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# Structure-guided negative pressure wound therapy (NPWT):

## personalised tissue biomodulation with an NPWT system in adults and older adults

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# Structure-guided negative pressure wound therapy (NPWT): personalised tissue biomodulation with an NPWT system in adults and older adults


## Abstract

**Background:** Negative pressure wound therapy (NPWT) has revolutionised the management of complex wounds via mechanisms such as microdeformation, angiogenesis and exudate control. However, its clinical effect has historically only been evaluated by qualitative and visual parameters. This study integrates near-infrared spectroscopy (NIRS) as a biofeedback tool to quantify physiological response to NPWT in real time.

**Objective:** This study aimed to quantitatively demonstrate the physiological and structural changes induced by an NPWT system in patients with complex wounds, measured using NIRS.

**Methods:** A prospective real-world observational study was conducted with a cohort of 23 patients with 33 wounds. Structural and physiological parameters were documented before and after NPWT treatment. Random-intercept mixed-effect statistical models and pre–post comparison tests were used to assess clinical and physiological significance.

**Results:** The data showed a progressive reduction in wound area and volume, accompanied by an increase in tissue oxygen saturation and a sustained decrease in deoxygenated haemoglobin. These findings, objectively quantified through NIRS as a real-time biofeedback tool, highlight the improvement in oxygenation and wound-bed perfusion and support the hypothesis of tissue biomodulation induced by NPWT.

**Conclusion:** The integration of NIRS redefines the clinical role of NPWT, allowing therapy to be customised based on specific physiological data. This combination represents a new frontier in precision wound medicine. The results of this study provide a foundation for a new generation of clinical decisions in advanced wound management.



## Keywords

**Negative pressure wound therapy, near-infrared spectroscopy, wound healing, perfusion, tissue oxygenation, biomodulation**


Patients living with hard-to-heal wounds represent a significant challenge for health systems globally, as these conditions directly affect quality of life, care burden and institutional costs.[1] Hard-to-heal wounds, such as vascular ulcers, pressure injuries and complex postoperative wounds, have traditionally been evaluated using observable structural parameters, such as area reduction, bed appearance or exudate reduction. While these indicators are clinically useful, they do not always capture the underlying pathophysiological processes that determine therapeutic success.

Negative pressure wound therapy (NPWT) has been one of the most significant advances in the management of complex wounds. Since its introduction by Morykwas and Argenta in 1997,[2] this therapy has been shown to present benefits at the cellular level, promoting angiogenesis, wound-bed contraction and fibroblast stimulation through mechanisms such as tissue microdeformation and modulation of interstitial pressure.[3,4] Consensus documents and systematic reviews have reinforced its clinical value in various aetiological contexts, from postoperative management to the prevention of complications in high-risk wounds.[3,5]

Despite these advances, a critical gap persists in clinical practice: the impossibility of quantifying the physiological response of tissues to treatment objectively and in real-time. The efficacy of NPWT has been predominantly evaluated qualitatively through the clinical course of wounds; however, therapeutic success depends not only on surface closure, but also on underlying biochemical, physical and cellular processes, such as perfusion, oxygenation, tissue remodelling and local inflammatory response. Various systematic reviews and consensus documents have pointed out these methodological limitations and the absence of objective physiological markers.[6–8] Recently, near-infrared spectroscopy (NIRS) has been proposed as a real-time feedback tool that allows for the quantification of oxygenation and perfusion, redefining the way wound healing is monitored.[9–12] The use of NIRS in the present study offers a solution to this limitation, allowing for real-time tracking of key biophysiological parameters, such as oxygenated haemoglobin ($HbO_2$), deoxygenated haemoglobin (Hb), tissue oxygen saturation ($StO_2$) and total haemoglobin (THb).

NIRS sensors were placed directly on the periwound skin adjacent to the NPWT dressing, allowing for repeated non-invasive measurements during each visit without interfering with therapy delivery. These markers reflect the functional status of the tissue and allow continuous

monitoring of biomodulation induced by advanced treatments such as NPWT.[13] The quantification of perfusion and oxygenation with NIRS in this study represents a significant step forward, since it enables treatment protocols for NPWT to be evidence-based and standardised. Even in centres without access to NIRS, the established correlation between structural wound changes and physiological responses can guide clinical decisions and facilitate reproducibility across diverse care settings.

This study is proposed as the first to quantitatively integrate the structural and physiological response of tissues to NPWT using NIRS. The current study presents a new model of personalised therapy based on biofeedback, where the treatment serves to both act and inform. The author proposes an operating model based on structural and phase-specific observation of the wound, called structure-guided NPWT, as an innovative and reproducible form of therapeutic personalisation.

## Pathophysiological basis and biomodulation

### Cellular mechanisms

NPWT exerts its therapeutic effect through a series of interrelated cellular mechanisms that synergistically contribute to the repair of injured tissue. Although it was initially conceived as a tool for exudate control, the impact of NPWT is multifactorial, ranging from direct mechanical stimulation to the modulation of the biochemical microenvironment of the wound, which is now known as the active process of biomodulation.

#### Micro tissue deformation

Tissue microdeformation is a biomechanical phenomenon induced by sub atmospheric pressure applied through the interface between the foam dressing and contact with the wound bed. This effect generates mechanical stimuli that promote the reorganisation of the cell cytoskeleton, stimulate the migration of keratinocytes and fibroblasts and promote the synthesis of collagen and the extracellular matrix.[2,4] These cell traction forces have been associated with greater proliferation and differentiation of cells in the wound bed, establishing a dynamic microenvironment that accelerates regeneration.

#### Negative pressure-induced angiogenesis

At the vascular level, NPWT significantly stimulates angiogenesis due to increased transcapillary pressure and mechanical stress on endothelial cells. This phenomenon has been described as a common adaptive mechanism in tissues subjected to moderate hypoxia, which stimulates capillary formation through local signals such as vascular endothelial growth factor (VEGF).[13] In the context of NPWT, this effect has been observed in clinical and experimental studies, such as a documented increase in local levels of interleukin-8 (IL-8) and VEGF in traumatic wounds treated with NPWT, suggesting activation of the pro-angiogenic cascade as part of the repair process.[14]

This phenomenon has also been corroborated by a description of how negative pressure can induce rapid angiogenesis in areas with compromised microcirculation, acting as a catalyst for the vascular recovery process.[3] In addition, NPWT has been shown to favour the recruitment of mesenchymal stem cells, which migrate to the site of injury in response to the mechanical gradient and release of local growth factors.[4] In animal models, NPWT has been demonstrated to increase local perfusion by 21–103%, depending on the level of pressure applied.[2] Subsequent studies have confirmed that induced angiogenesis is both structural and functional, with vessels improving the transportation of oxygen and nutrients to ischaemic tissues.[15]

#### Cell migration and recruitment of repair cells

NPWT also promotes directed cell migration, a key process for wound bed repopulation. The migration of fibroblasts, keratinocytes and endothelial cells to the affected area is favoured by the physical gradients created by suction, as well as the local release of cytokines and chemotactic factors.[3,4]

Tissue remodelling is influenced by the mechanical and chemical balance generated by NPWT, which regulates the deposition of new connective tissue and the organisation of collagen.[3,4] This interaction between mechanical stimulus, biochemical signalling and cell migration constitutes the core of biomodulation.[16] In addition, there is an increase in the infiltration of progenitor cells and mesenchymal stem cells, which actively participate in tissue regeneration and revascularisation.[3]

#### Modulation of exudate and wound microenvironment

Another essential component of the cellular effect of NPWT is the modulation of exudate, which allows the volume of inflammatory fluid accumulated in the wound to be controlled, reducing oedema and interstitial pressure.[2,3] This continuous removal of exudate helps to decrease the local concentration of matrix metalloproteinases (MMPs), free radicals and cell-degradation products, which interfere with healing.[4,16]

NPWT modulates the biochemical profile of the wound by reducing the concentration of pro-inflammatory mediators in the exudate and promoting the transition to a regenerative profile. This includes the decrease of MMPs and catabolic cytokines, allowing for greater stability of deposited collagen and improved integrity of the extracellular matrix.[4,16] This process is key in the transition from a hard-to-heal wound to a progressively-healing wound, by promoting a biologically active environment.[1] By improving tissue oxygenation and reducing the proteolytic load on the environment, NPWT restores a favourable balance for cell regeneration and a transition to the proliferative phase of the healing process.[1,16]

## Biochemical changes during biomodulation

During application of NPWT, the wound microenvironment undergoes biomechanical modifications. These changes affect the inflammatory mediator profile, redox balance, enzyme activity and oxygen availability, all of which are essential for efficient and sustained healing.[3,13,14]

## Vascular endothelial growth factor induction and molecular angiogenesis

NPWT stimulates the expression of VEGF through tissue microdeformation, mechanical stress and moderate localised hypoxia. NPWT increases local levels of VEGF traumatic wounds, promoting the formation of new, functional blood vessels.[14] The therapy also acts as a catalyst for vascular recruitment, even in tissues with compromised perfusion.[3] In the context of healing in patients with comorbidities, studies have linked angiogenic stimulation with a simultaneous reduction in oxidative stress and an improvement in oxygen bioavailability.[17,18] This relationship between the VEGF pathway, redox regulation and anti-inflammatory effect supports the current approach of using NPWT as comprehensive physiological modulation therapy.

## Increase in interleukin-8 and its role in pro-reparative inflammation

IL-8 is a pro-inflammatory cytokine that plays a dual role, as it promotes neutrophil and monocyte chemotaxis as well as inducing secondary angiogenesis. NPWT treatment significantly increases IL-8 levels, suggesting selective activation of the inflammatory-reparative axis.[14] This type of response is especially relevant in hard-to-heal wounds, where the inflammatory response is usually dysregulated. The balance between IL-8 and other proinflammatory cytokines can be a key determinator for progressing from pathological to regenerative inflammation.[3,17]

## Decrease in matrix metalloproteinases

MMPs, especially MMP-2 and MMP-9, are chronically elevated in hard-to-heal wounds. These enzymes degrade collagen, fibronectin and other essential components of the extracellular matrix, interfering with tissue regeneration. NPWT can reduce local concentrations of MMPs by evacuating exudate and decreasing oxidative stress.[4] In parallel, pH restoration and free radical reduction in hard-to-heal wounds are associated with indirect inhibition of MMPs.[17] This suggests that NPWT not only removes MMPs mechanically, but also modulates the biochemical environment that induces their expression.

## Decrease in chronic catabolic cytokines

Cytokines, such as tumour necrosis factor alpha and interleukin-1 beta, and other pro-inflammatory molecules are frequently elevated in stagnant wounds. These perpetuate cell damage, inhibit fibroblast and keratinocyte migration, as well as alter angiogenesis. The application of sub atmospheric pressure reduces the concentration of these cytokines by removing exudate and restoring local perfusion.[2,3] The combination of antioxidant intervention and pH restoration has been demonstrated to significantly reduce inflammatory mediators in models with high oxidative stress.[17]

## Regulation of oxidative and nitrosative stress

Continuous exposure to free radicals is one of the limiting factors in the healing of complex wounds. The antioxidant compounds 3,4-dihydroxyphenylglycol and hydroxytyrosol have been demonstrated to upregulate markers such as glutathione and total antioxidant capacity, while decreasing 8-hydroxy-2-deoxyguanosine, thiobarbituric acid reactive substances and nitrotyrosine.[18] Although these studies were not conducted with NPWT, their results can be applied to the context of an inflamed and oxidised microenvironment, such as in hard-to-heal wounds. By controlling exudate, improving oxygenation and reducing acidic pH, NPWT activates endogenous antioxidant pathways, which may indirectly facilitate cellular repair and progression from inflammatory to proliferative phases.[1,16,17]

## Physiological hypothesis

Negative pressure triggers a complex physiological response, producing a regenerative environment characterised by improved microvascular perfusion, increased tissue oxygenation, decreased oxidative stress and active cell reorganisation. These processes, so far described experimentally or qualitatively, can be objectively measured using NIRS, creating scope for the personalisation of biofeedback-guided therapy.

## Increased microvascular tissue perfusion

NPWT improves perfusion by reducing interstitial pressure, opening collapsed capillaries and generating angiogenic stimuli. Perfusion can increase up to 103%, depending on the level of pressure applied.[2] This effect helps to preserve marginal microcirculation in burn wounds.[15] Reinforcing this hypothesis, NPWT has been shown to act as a catalyst for revascularisation in compromised areas.[3] In addition, studies using NIRS have shown progressive increases in THb—a proxy for microvascular blood volume—together with improvements in $StO_2$ during NPWT.[9,10]

## Improved tissue oxygenation and mitochondrial capacity

The main implication is that NPWT improves oxygenation and perfusion, which directly supports wound progression from the inflammatory to the proliferative phase. The increase in perfusion enables increased oxygen delivery to the affected tissue, which is critical in the transition to proliferative phases. Moderate hypoxia activates neovascularisation pathways that improve functional oxygenation of reparative tissue.[13] Measurements with NIRS have demonstrated a sustained increase in tissue $StO_2$ levels following the application of NPWT.[16] Oxygenation levels measured with NIRS correlate with improved clinical outcomes, granulation quality and perilesional viability.[9] These effects are enhanced in microenvironments with optimal pH and low oxidative stress.[17,18]

## Negative pressure-induced cell reorganisation

The microdeformation generated by sub atmospheric pressure stimulates mechano-sensitive receptors and intracellular pathways, such as mitogen-activated protein kinase, focal adhesion kinase and integrins, which activate the migration and differentiation of fibroblasts, keratinocytes and endothelial cells. This process activates

genes associated with extracellular matrix synthesis, collagen remodelling and growth factor release.[4,16] Cell reorganisation can be further accelerated with near-infrared-responsive biomaterials, which enable on-demand local drug release and activation of intracellular biochemical pathways.[22,23] This concept is distinct from NIRS, which is used to monitor oxygenation and perfusion.

### Quantitative validation with near-infrared spectroscopy

Emerging technologies, such as hydrogels and near-infrared-photoactivated dressings, are being developed to release drugs under spectroscopic control.[10,11] NIRS allows the quantification of Hb, $HbO_2$, $StO_2$ and THb in real time. This technology represents a form of clinical biofeedback, capable of objectively correlating the therapeutic effect of NPWT with tissue physiology. This type of monitoring allows therapeutic personalisation based on tissue dynamics.[9]

## Proposed clinical model: structure-guided negative pressure wound therapy

### Knowledge gap

Despite technological advances in NPWT, a significant gap persists in clinical evidence related to real-time physiological quantification of therapeutic effects. Existing studies have focused on structural or morphological parameters, such as reduction in wound size, presence of granulation tissue or closure time, without integrating dynamic physiological indicators such as oxygenation, perfusion and cell reorganisation.[5–7]

Although there are promising results with NPWT, the quality of the evidence still faces limitation:

- Absence of real-time physiological quantification, with no clinical study to date having simultaneously measured the structural and functional effects of treatment, as proposed in this study with combined NIRS[5,7,19]
- Methodological limitations and lack of physiological control, with most previous studies being retrospective, having significant heterogeneity and not incorporating perfusion or tissue oxygenation parameters as evaluation or inclusion criteria[20–22]
- Explicit call for more robust and personalised studies, with international guidelines and methodological recommendations advocating for more structured research that includes objective tools, advanced technologies and integrative clinical models.[5,6,22,23]

The new-generation RENASYS◊ EDGE Negative Pressure Wound Therapy System (Smith+Nephew, Hull, UK) has documented its ease of use and functional improvements in wounds,[24] but there remains no published evidence directly linking these improvements to physiological biomarkers monitored in real time. The physiological experience of the patient has also not been systematically documented beyond qualitative studies.[25] In parallel, recent publications confirm that the wound environment, including oxygenation, pH, oxidative stress and microvascular dynamics, is a key descriptor of clinical evolution.[9,26,12] The incorporation of technologies such as NIRS and dermal pH sensors position the present study as a pioneering model in personalised wound medicine guided by biofeedback.[9–11,27]

This study proposes the first quantitative clinical approach that combines structural measurement with continuous physiological monitoring in complex wounds, using NIRS to capture perfusion and oxygenation data that support or reorient therapeutic decisions in real time. In addition to these physiological gaps, the study identifies a critical absence of operational models that guide the therapeutic adjustment of NPWT according to the structural evolution of the wound. This study quantifies oxygenation and validates a practical model of therapeutic personalisation based on healing and systematic clinical observation, applicable even in environments without advanced technology.

## Differential value of the study

The present study offers novel conceptualisation and preliminary validation of the structure-guided NPWT model, which proposes to personalise negative pressure treatment not only based on physiological parameters, but also through active morphological reading of the wound, adjusting therapies, dressings and pressure modes. Structure-guided NPWT is an advanced clinical model that overcomes the historical methodological limitations of NPWT studies. Its differential value lies in the ability to correlate, objectively and quantitatively, the visible structural changes in the wound with physiological parameters measured in real time using NIRS.

This study proposes the simultaneous evaluation of structural (area, depth and volume) and physiological (Hb, $HbO_2$, $StO_2$ and THb) variables, applying NIRS monitoring before, during and after NPWT. It allows the differentiation of a wound that closes without adequate oxygenation, creating the opportunity to detect subclinical stagnation in apparently stable but biochemically unfavourable wounds.[9,16–18]

The study also introduces the concept of smart pressure, referring to a therapeutic system that simultaneously acts and monitors, enabling individualised adjustments. This framework is part of precision wound medicine,[28] aligned with international expert recommendations, and conceptually connected to emerging technologies such as near-infrared-responsive biomaterials.[10,11] Importantly, smart pressure does not depend exclusively on advanced technologies, as the core value lies in the correlation between structural changes and physiological responses, which can guide reproducible protocols even in health systems with limited resources. In this way, it constitutes a step towards responsive therapy, where wound structure and quantifiable data support precision-based decisions.

## Methodological innovation of the study

The main innovation of this work is based on the systematic integration of NIRS to the NPWT algorithm. This has not been standardised or systematically applied in clinical trials or observational cohorts until now. By combining NIRS with NPWT, this study lays the groundwork for a clinical algorithm that can be replicated in various contexts,

reinforcing the applicability of the structure-guided NPWT model as a personalised medicine tool.

The present study was conducted in active clinical scenarios of ambulatory and inpatient care, which allows for the verification of the feasibility and reproducibility of the use of NIRS with the NPWT system.[16,24,25] This is a real-world observational analysis of patients with hard-to-heal, complex or recalcitrant wounds. The protocol follows methodological guidelines proposed by the European Wound Management Association (EWMA)[6,5,29–31] and Cochrane Wounds Group (CWG),[32,20,7,8] incorporating objective measures, clear inclusion criteria, functional and structural endpoints and robust statistical analysis, with validated software and internal quality control.

# Objectives

## Primary objective

The primary objective of this study is to quantify the therapeutic effect of next-generation NPWT using structural and biophysiological parameters measured with NIRS, and to integrate this quantification with the structure-guided NPWT model based on the clinical morphological evolution of each wound.

## Secondary objectives

### Evaluating the evolution of tissue oxygenation and perfusion

Local oxygenation is an essential determinant of the healing process. Elevated $StO_2$, $HbO_2$ and THb, along with progressive reduction in deoxygenated Hb, have been associated with improved tissue perfusion and vascular regeneration.[9,13,27] NPWT positively modulates these pathophysiological mechanisms, promoting the oxygen gradient necessary for collagen synthesis, cell proliferation and activation of factors such as VEGF.[3,13–16]

### Correlating physiological changes with reduction in wound size

Studies that analyse changes in volume, depth or area of wounds often lack direct correlation with physiological parameters. The combination of NIRS data with clinical measurements allows for the establishment of quantitative relationships between biofunction and morphological evolution, which has not yet been documented in an integrated manner.[9,11,24,25,33]

### Exploring response patterns

Response pattern stratification was based on EWMA[6,5,29-31] and CWG[32,20,7,8] recommendations on the need to personalise wound management according to their aetiology, physiological response and complementary therapies. The response patterns explored in the current study include:

- Wound aetiology, including pressure injuries, diabetic foot ulcers, surgical wounds, traumatic wounds or vascular wounds[5,34,35]
- Anatomical location, including lower-limb, plantar, sacral or trunk wounds[16]
- Adjuvant therapies, including silver, collagenase and cross-linked foam dressings,[34,36–39] as well as cellular, acellular and matrix-like products (CAMPs)[40]
- Predominant healing phase, whether inflammatory, proliferative or epithelial, and phase-specific therapeutic adjustment, as a basis for validating a structural clinical algorithm of therapeutic personalisation.

## Added value of design

The present study incorporates longitudinal measurement with clinically validated sensors, [41,42] impact evaluation according to aetiology and adjuvant therapies,[13,43,44] and the application of devices approved for clinical use.[41,45,46] Beyond the quantitative use of NIRS, the study proposes and validates an applied structural observation model that allows NPWT to be progressively adjusted according to the morphological phase of the wound. This methodological proposal, termed structure-guided NPWT, represents an innovation applicable to multiple clinical scenarios, even without access to advanced physiological monitoring tools.

# Methods

## Study design

A prospective, real-world observational study was carried out in a clinical setting specialised in the management of complex wounds. This design reflects a real-world evidence approach, ensuring that findings are applicable to daily clinical practice beyond the controlled conditions of randomised trials, while maintaining internal quality standards.[6]

The study evaluated the structural and physiological evolution of wounds treated with the NPWT system, complemented by real-time monitoring of tissue oxygenation and perfusion through NIRS.[9] The integration of NIRS into the study design allowed the therapeutic effects of NPWT to be objectively quantified, providing physiological biofeedback beyond traditional structural parameters such as wound area, volume or tissue type.[10,12]

The protocol was aligned with the methodological recommendations of major international organisations, including EWMA[6,5,29–31] and CWG.[7,8,20,32] It incorporated objective measures, predefined inclusion and exclusion criteria, functional and structural endpoints, and robust statistical analyses performed with validated software (SAS version 9.4, Cary (NC), US; R version 4.3.2, Murray Hill (NJ), US). Internal quality control was ensured through systematic cross-checking of clinical records, NIRS readings and serial photographic documentation, in accordance with best practice guidelines for wound research.[6]

## Population and sample

A total of 23 patients were included, both male and female, aged between 25 and 71 years, diagnosed with hard-to-heal wounds of multiple anatomical locations and aetiologies, including pressure ulcers, surgical wounds, diabetic foot ulcers and traumatic wounds. A total of 33 wounds were treated, since several patients had more than one lesion located in different anatomical areas. This approach offers a significant advantage in controlling shared systemic factors in the same patient and allows for the examination of scarring behaviours in different tissues under similar

conditions.[47] This reinforces the clinical complexity of the cohort and allows for differential patterns of response to be explored in greater depth.

Patients older than 21 years with complex hard-to-heal wounds were eligible for inclusion. Exclusion criteria comprised decompensated comorbidities, active immunosuppression, treatments significantly altering perfusion (e.g., intravenous vasopressors) and untreated osteomyelitis, in line with recognised contraindications for NPWT described in international guidelines.[5]

## Negative pressure wound therapy treatment delivery

NPWT therapy was applied using RENASYS EDGE◊ Negative Pressure Wound Therapy System (Smith+Nephew, Hull, UK), under standardised protocols for the application of traditional NPWT, with parameters clinically adjusted to the characteristics of each wound according to institutional protocol and international recommendations.[24] The evaluation was carried out using the Snapshot (Kent Imaging, Calgary, Canada) NIRS system, before the intervention and serially during follow-up, analysing the following quantitative parameters: Hb, $HbO_2$, $StO_2$ and THb.[9–11]

Records were taken before the start of treatment and during clinical follow-up, according to a pre-established and systematic schedule.[9,11,16,17,27] The clinical team also applied a phase-specific therapeutic algorithm based on structural observation (wound size, tissue types, edges and exudate), which allowed the mode and pressure of NPWT to be customised according to the healing phase (inflammatory, proliferative and epithelial). This approach reinforces the applicability of structure-guided NPWT even without NIRS.

Clinical assessments were scheduled twice weekly during the initial phase. Once wounds achieved approximately 40% reduction in area, the follow-up frequency was reduced to once weekly, according to exudate levels and clinical evolution. This flexible scheme allowed close monitoring without overburdening patients, ensuring that NIRS and structural data were consistently collected at each visit.

Use of NPWT in wounds with devitalised tissue followed international recommendations (FDA,[48] EWMA,[5] Wounds International[49]) contraindicating NPWT in the presence of spreading/systemic infection over dry, firm, adherent, dark brown or black necrotic tissue (eschar). NPWT with instillation therapy and dwelling time is reserved for scenarios with eschar or heavy bioburden. However, NPWT can be safely used over soft, moist or fibrinous slough. Following the 2024 Debridement Consensus[50], this use should be a coadjuvant form of mechanical debridement in combination with other recognised methods (autolytic, osmotic, enzymatic), as part of the debridement continuum. This followed a phased protocol: removal of accessible non-viable tissue at baseline and serial mechanical debridement at each dressing change, combined with autolytic/enzymatic or osmotic methods when a more conservative approach was safer. Synergistic use of NPWT for a mechanical debriding effect should enhance wound bed preparation and accelerate progression to viable tissue, thus optimising resources, avoiding unnecessary surgical interventions and promoting safer, more efficient clinical outcomes.[4,5,50,55]

## Study variables

Structural variables included wound area ($cm^2$) and wound volume ($cm^3$), both with rectangular and elliptical estimates, as well as presence of granulation tissue and slough. Exudate level was assessed using a standardised clinical scale (none, scant, low, moderate, high), and consistency was also recorded (thin or thick) according to international wound assessment guidelines.[39,40] Physiological variables (measured by NIRS) included Hb (µM or g/L), $HbO_2$ (µM or % of total haemoglobin), $StO_2$ (%) and THb (µM or g/L).

NIRS sensors were placed directly on the periwound skin adjacent to the NPWT dressing, allowing for repeated non-invasive measurements during each visit without interfering with therapy delivery. Complementary clinical variables included wound type, aetiology, anatomical location, adjuvant therapies (e.g., silver dressings, collagenase, CAMPs)[10,35] and follow-up time (measured in days to closure or clinical endpoint). Relevant sociodemographic and clinical variables (age, sex, main diagnosis, comorbidities) were also collected.

## Evaluation and registration procedures

All data were collected by trained clinical staff, with informed consent from the participants. A systematised and standardised documentation protocol was used, including digital clinical photography, manual measurement with sterile template and NIRS readings. This multidimensional integration allows the morphological evolution of the wound and its internal physiological changes to be documented simultaneously, in line with methodological recommendations for clinical studies in wounds.[47]

## Statistical analysis

Data analysis was performed using quantitative techniques with specialised statistical software (SAS version 9.4, Cary (NC), US; R version 4.3.2, Murray Hill (NJ), US). The following tests were applied:

- Parametric and non-parametric tests according to the distribution of the data (Kolmogorov-Smirnov, Shapiro-Wilk)
- Repeated measures modelling using random-intercept mixed-effect models to evaluate the longitudinal evolution of NIRS and structural variables.

A *P* value of less than 0.05 was considered statistically significant. Data integrity and bias control were monitored by cross-checking clinical records and serial photographs, in accordance with the methodological quality principles recommended in hard-to-heal wound studies.[6,47]

## Ethical approval and regulatory framework

The study was conducted in compliance with the principles of the Declaration of Helsinki.[51] All participants signed an informed consent form, and the data were anonymised to

protect confidentiality. The treatment protocol with NPWT corresponded to the standard of care in the accredited clinical setting, and no patient's wound care plan was altered because of study participation. The institutional ethics committee reviewed the project and determined that, as a real-world observational case series where standard of care was maintained and no additional risk was introduced, formal trial approval was not required. Data collection and monitoring were supported by the centre's medical management, in line with quality and clinical safety standards for applied wound research.

## Results

Dynamic changes in the area, volume and depth of the lesions were documented using validated measurements, NIRS in 27 of the 33 wounds and systematic photographic recording. This approach allowed for the quantification of structural evolution and validation of the phase-specific intervention model from clinical observation, the basis of the concept of structure-guided NPWT.

This therapeutic approach integrated NPWT with other advanced modalities—such as antimicrobial dressings, CAMPs, membranes and enzymes—enabling the analysis of macrostructural evolution under diverse clinical conditions. The data revealed a significant reduction in wound size, a high wound closure rate (73%) and a favourable physiological response that reinforce the active structural effect of the NPWT system beyond mechanical sealing.

## Patient demographics

The study included 23 patients with a mean age of 53 years (standard deviation (SD)=11; range=25–71). The age distribution was relatively homogeneous, with half of participants aged from 45–62 years, with fewer women (39%) than men (61%) (*Box 1*).

## Risk factors

The most prevalent comorbidity among participants was diabetes (65%) followed by hypertension (57%) and peripheral vascular disease (30%). Obesity (22%) and tobacco use (17%) were also observed, while hyperlipidaemia was less frequent (4%). These findings reflect a population with multiple vascular and metabolic risk factors commonly associated with delayed wound healing (*Tables 1* and *2*).

## Wound location and type

The wounds were distributed across 10 anatomical locations, the most frequent being the foot (35%) and the leg (17%). Less common sites included the abdomen (13%), multiple locations (8.7%) and single cases in the back, chest, finger, knee, pelvis and wrist (*Table 3*). Regarding wound type, dehisced surgical wounds (43%) and traumatic wounds (22%) predominated, followed by infection-related wounds (13%) and diabetic foot ulcers (8.7%) (*Table 4*). Other wound types, including necrotising fasciitis, post-infectious amputation wounds and pressure injuries, were less frequent. Although peripheral arterial disease was a common comorbidity in this cohort, no wounds were classified as primary arterial ulcers, so this category was not reported as a separate aetiological group.

**Box 1. Demographic characteristics (n=23)**

**Age**
- Mean, 53
- Standard deviation, 11
- Median, 54
- Interquartile range, 45–62
- Range, 25–71

**Sex, n (%)**
- Female, 9 (39%)
- Male, 14 (61%)

**Table 1. Main risk factors reported (n=23)**

| Characteristic | n (%) |
|---|---|
| Diabetes | 15 (65%) |
| Hypertension | 13 (57%) |
| Peripheral vascular disease | 7 (30%) |
| Obesity | 5 (22%) |
| Tobacco use | 4 (17%) |
| Hyperlipidaemia | 1 (4.3%) |

**Table 2. Frequency of additional risk factors listed as free text options (n=13)**

| Characteristic | n |
|---|---|
| Neuropathy | 4 |
| Renal failure | 2 |
| Asthma | 1 |
| Hepatic failure | 1 |
| Immunocompromised | 1 |
| Organ transplant | 1 |
| Osteoarthritis | 1 |
| Osteomyelitis | 1 |
| Tinea pedis | 1 |

## Wound area and volume

Changes in wound area and volume were used to quantify the structural response to treatment (*Table 5* and *Figure 1*). Clinical follow-up ranged from 7–70 days per wound (mean 28 days). Trajectories of progressive structural reduction were identified, with reductions already occurring from the second visit (up to 9 days later) and consolidation of the closure in weeks 3–5. While individual wound trajectories were documented and analysed, the following section presents aggregated results (means and percentages) to summarise overall structural evolution across the cohort. In most cases, notable reductions in wound area could be clearly observed before day 14. At the first visit, the median wound length was 2.3 cm (Q1–Q3, 2.0, 4.0) and the median width 2.5 cm (Q1–Q3, 1.5, 4.0). Median wound depth was 0.5 cm (Q1–Q3, 0.4, 1,1), although five wounds could not be measured due to devitalised coverage. The estimated median baseline wound area, using elliptical approximation, was 4.7 $cm^2$ (Q1–Q3, 2.4, 11.8), and the median wound

**Table 4. Wound type at start of study (n=23)**

| Wound type | n (%) |
|---|---|
| Dehisced surgical wound | 10 (43%) |
| Traumatic wound | 5 (22%) |
| Post infection, incision and drainage | 3 (13%) |
| Diabetic foot ulcer | 2 (8.7%) |
| Necrotising fasciitis | 1 (4.3%) |
| Post infection with amputation | 1 (4.3%) |
| Pressure injury | 1 (4.3%) |

volume was 4.2 $cm^2$ (Q1–Q3, 1.3, 8.7).

Using mixed-effects modelling, the estimated mean daily reduction in wound area was 5.61% (95% confidence interval (CI) 4.88–6.34; *P*<0.001). This trend was consistent across both rectangular and elliptical approximations. By the last visit, 73% of wounds had achieved complete closure, with the remaining cases showing marked reduction in area and volume (*Table 6*).

Unlike previous studies that focused exclusively on structural outcomes (area, volume, closure time), the present study incorporated physiological parameters measured with NIRS ($StO_2$, Hb, $HbO_2$, THb). This dual evaluation allowed the therapeutic effects of NPWT to be quantified through real-time functional tissue responses, reinforcing the concept of structure-guided NPWT.

## Wound edge and wound bed structure

At baseline, all wounds had non-advancing edges, most wound beds were predominantly devitalised (56%), with the remainder largely granulation tissue (42%). By the second visit, 100% of wounds demonstrated advancing edges, with a marked shift toward granulation tissue (69%). At the final visit, 73% of wounds had healed, and the remaining open wounds predominantly showed advancing edges with granulation tissue, while slough had resolved completely (*Table 7*).

## Exudate

At baseline, 69% of 33 wounds presented with a high level of exudate and most wounds had thick exudate (67%). By the second visit, wounds with high exudate had decreased to 53%, accompanied by an increase in wounds with thin exudate. At the final visit, nearly all unhealed wounds had no, scant or low exudate, and the majority of exudate present was thin (88%), indicating a significant improvement in wound fluid management over time (*Tables 8* and *9*).

## Physiological characteristics

From baseline to the last visit, Hb decreased from 41.0 μM to 29.9 μM; $HbO_2$ increased from 82.6 μM to 140.6 μM; $StO_2$ increased from 60.1% to 80.2%; and THb increased from 123.6 μM to 170.4 μM, indicating a consistent improvement across visits (*Table 10*).

Longitudinal mixed-effects models confirmed statistically significant trends over time: Hb decreased by 0.308 g/L per day (95% CI –0.463 to –0.153; *P*<0.001); $HbO_2$ increased by 2.133% per day (95% CI 1.517–2.750; *P*<0.001); $StO_2$ increased by 0.637% per day (95% CI 0.428–0.847; *P*<0.001); and THb increased by 1.804 g/L per day (95% CI 1.205–2.403; *P*<0.001).

Although the cohort included 33 wounds, the number of observations differed across visits (28 at baseline, 16 at the second visit and 24 at the last visit). This variation was due to the fact that not all wounds could be measured with NIRS at every visit given technical limitations (e.g., motion artefacts, dressing interference, local humidity) or because some wounds achieved closure before completing the full monitoring schedule. However, all 33 wounds were clinically assessed throughout the study, ensuring consistency in structural follow-up.

## Comparison between patients with one vs multiple wounds

Of the participants, 87% had a single wound, but three patients (13%) had multiple lesions (up to eight) (*Table 11*). Structural reductions were seen in patients with one wound and multiple wounds, suggesting robust efficacy of the system even in complex clinical contexts. All wounds, regardless of whether patients had a single or multiple lesions, were treated using the same NPWT system under a standardised structure-guided protocol, ensuring methodological consistency across the cohort.

Most patients had a single wound (87%), while a minority presented with multiple wounds (13%); the presence of multiple wounds did not appear to impact wound closure rates. Importantly, this analysis highlights one of the distinctive contributions of the present study: the integration of NIRS as a tool for real-time biofeedback. By quantifying physiological parameters such as Hb, $HbO_2$, $StO_2$ and THb in parallel with structural wound evaluation, it was possible to capture the dynamic physiological response to NPWT. This dual structural-physiological approach reinforces the robustness of the results and differentiates the study from previous reports that relied mainly on qualitative or structural indicators.

# Discussion

## Global summary of structural evolution

In addition to the quantitative changes, repetitive morphological patterns were identified that allowed for personalised adjustment according to the phase of healing observed. This reinforces the clinical feasibility of a therapeutic algorithm based on structural observation, without relying exclusively on advanced technologies.

The wounds included in this analysis were located in a range of anatomical locations and had received different types of therapy. All 23 patients and 33 wounds evaluated showed a significant and sustained reduction in area, volume and depth, with an overall clinical closure rate of 73%. This consistent improvement suggests that NPWT facilitates active structural biomodulation.

The results indicate a positive modulation of the microstructural environment, acceleration of granulation and effective tissue reorganisation, beyond occlusive sealing. The NPWT system, in combination with personalised therapeutic strategies and a phase-specific intervention

**Table 5.** Estimated wound areas and volumes by visit (n=33)

| Measurement | Visit | Mean (SD) | Median (Q1– Q3) | Min to Max |
|---|---|---|---|---|
| Wound area in $cm^2$ (rectangular approximation) | First | 11.55 (13.15) | 6.00 (3.00–15.00) | 0.75–54.00 |
| | Second | 11.55 (13.15) | 6.00 (3.00–15.00) | 0.15–46.64 |
| | Last | 2.04 (6.91) | 0.00 (0.00–0.04) | 0.00–30.00 |
| Wound area in $cm^2$ (elliptical approximation) | First | 9.07 (10.33) | 4.71 (2.36–11.78) | 0.59–42.41 |
| | Second | 6.72 (9.13) | 2.83 (1.18–8.84) | 0.12–36.63 |
| | Last | 1.61 (5.43) | 0.00 (0.00–0.03) | 0.00–23.56 |
| Wound volume in $cm^3$ (rectangular approximation) | First | 12.34 (17.33) | 5.40 (1.70–11.08) | 0.53–60.00 |
| | Second | 6.86 (11.55) | 1.87 (0.51–5.40) | 0.05–45.00 |
| | Last | 1.06 (4.36) | 0.00 (0.00–0.00) | 0.00–24.00 |
| Wound volume in $cm^3$ (elliptical approximation) | First | 9.69 (13.61) | 4.24 (1.34–8.70) | 0.41–47.12 |
| | Second | 5.39 (9.07) | 1.47 (0.40–4.24) | 0.04–35.34 |
| | Last | 0.83 (3.42) | 0.00 (0.00–0.00) | 0.00–18.85 |

Note: First visit=day 0/baseline; second visit=day 2–9; last visit=day 7–70 (includes visit where wound healed)

**Figure 1.** Estimated wound area reduction over time (mixed-effects model; ribbon shows 95% confidence interval; slope P<0.001; one line=one wound)

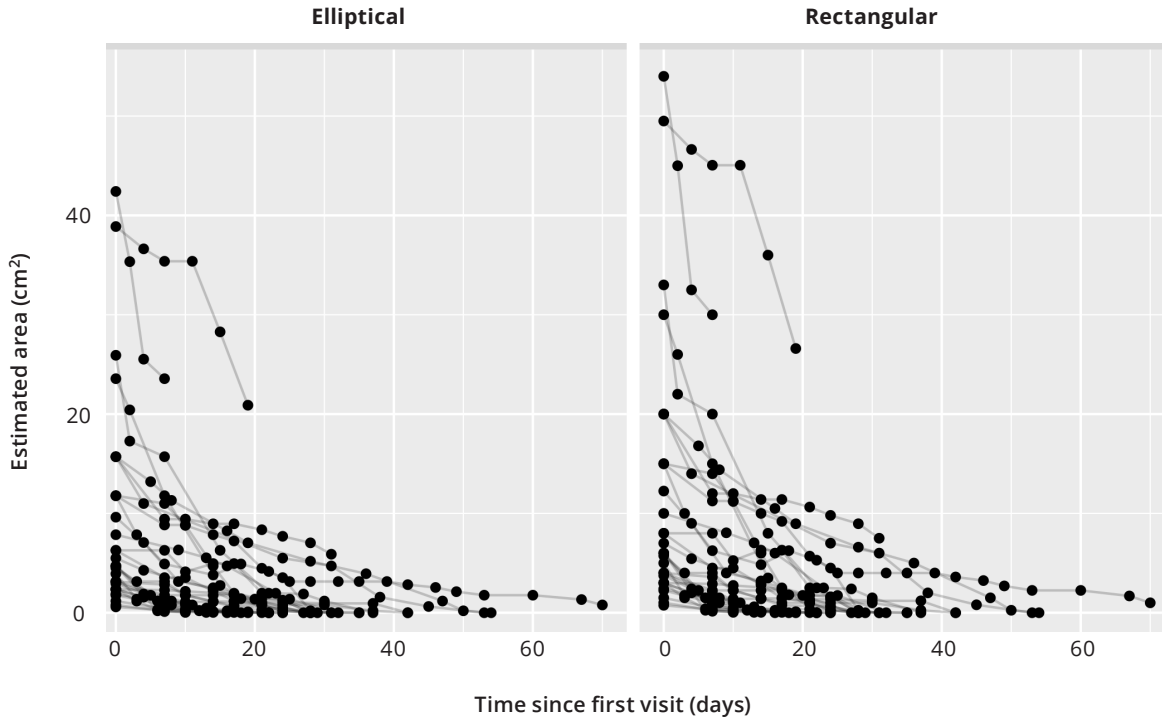



**Table 6.** Changes in wound areas and whether wound closed by last visit (n=24)

| Characteristic | Mean (SD) | Median (Q1–Q3) | Range |
|---|---|---|---|
| Absolute area change, $cm^2$ | 7.5 (6.8) | 4.7 (2.4–11.8) | 0.5–25.9 |
| Area change, % | 93 (15) | 100 (99–100) | 44–100 |
| Time since first visit, days | 28 (14) | 28 (19–32) | 7–70 |

model based on structured clinical observation, is positioned as a high-impact tool in the advanced management of complex wounds. These findings support the use of a specific structure-guided NPWT system, where therapy is progressively adjusted to wound morphology.

## Comparison with previous literature

The findings obtained in this observational study show an average wound area reduction of 93%, with a median closure of 100% and a clinical closure rate of 73%. The wounds were observed for periods ranging from 7–70 days,

**Table 7.** Wound edge and wound bed structure by visit, n (%)

| Characteristic | Category | First visit, n=32 | Second visit, n=32 | Last visit, n=33 |
|---|---|---|---|---|
| Wound edge | Non-advancing | 31 (100%) | 0 (0%) | 0 (0%) |
| | Advancing | 0 (0%) | 31 (100%) | 9 (27.27%) |
| | NA, healed* | NA | 0 | 24 (72.73%) |
| | Unknown | 1 | 1 | 0 |
| Wound bed structure majority | Epithelialisation | 0 (0%) | 1 (3.2%) | 0 (0%) |
| | Granulation | 13 (42%) | 22 (69%) | 9 (27.27%) |
| | Devitalised | 18 (56%) | 9 (29%) | 0 (0%) |
| | Tendon | 1 (3.2%) | 0 (0%) | 0 (0%) |

*0 cm width and length

**Table 8.** Exudate level and consistency by visit, n (%)

| Characteristic | Category | First visit, n=33 | Second visit, n=33 | Last visit, n=33 |
|---|---|---|---|---|
| Exudate level | None | 0 (0) | 1* (3.0) | 2 (6.0) |
| | Scant | 0 (0) | 0 (0) | 5 (15.2) |
| | Low | 7 (22) | 8 (25) | 1 (3.0) |
| | Medium | 3 (9.4) | 7 (22) | 2 (6.0) |
| | High | 22 (69) | 17 (53) | 1 (3.0) |
| | Unknown | 1 | 0 | 0 |
| | NA, healed† | NA | 0 | 22 (66.7) |
| Exudate consistency | Thin | 11 (33) | 16 (50) | 7 (88) |
| | Thick | 17 (67) | 16 (50) | 1 (13) |
| | Unknown | 0 | 1 | 2 |

*Wound unhealed as width/length >0 cm at second assessment/ †NA, healed is imputed when width and length=0 cm

**Table 9.** Change in exudate level from start to end of treatment, n (%)

| Visit | | Last visit | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | High | Medium | Low | Scant | None | NA, healed | Total |
| First visit | High | 1 (100%) | 2 (100%) | 1 (100%) | 0 | 0 | 18 (85.71%) | 22 (68.75%) |
| | Medium | 0 | 0 | 0 | 0 | 1 (50%) | 2 (9.52%) | 3 (9.38%) |
| | Low | 0 | 0 | 0 | 5 (100%) | 1 (50%) | 1 (4.76%) | 7 (21.88%) |
| | Scant | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | None | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | NA, healed | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Total | 1 (100%) | 2 (100%) | 1 (100%) | 5 (100%) | 2 (100%) | 21 (100%) | 32 (100%) |

**Table 10.** Physiological characteristics by visit

| Characteristic | Visit | Mean (SD) | Median (Q1–Q3) | Range |
|---|---|---|---|---|
| Tissue oxygen saturation | First, n=28 | 60.1 (19.7) | 66.0 (54.0–73.5) | 1.0–84.0 |
| | Second, n=16 | 71.3 (10.7) | 73.0 (67.0–78.0) | 45.0–86.0 |
| | Last*, n=24 | 80.2 (7.9) | 81.0 (76.5–85.0) | 63.0–92.0 |
| Haemoglobin | First, n=28 | 41.0 (13.3) | 39.5 (33.5–47.1) | 21.9–90.2 |
| | Second, n=16 | 32.1 (5.7) | 32.7 (27.9–36.9) | 20.8–40.0 |
| | Last*, n=24 | 29.9 (6.7) | 32.0 (26.4–33.6) | 15.5–39.4 |
| Oxyhaemoglobin | First, n=28 | 82.6 (43.9) | 68.0 (54.9–113.3) | 0.8–161.9 |
| | Second, n=16 | 99.6 (40.1) | 95.9 (79.3–119.4) | 45.8–204.2 |
| | Last*, n=24 | 140.6 (47.2) | 132.2 (113.7–183.1) | 50.7–222.9 |
| Total haemoglobin | First, n=28 | 123.6 (41.7) | 106.8 (93.1–149.8) | 53.7–211.6 |
| | Second, n=16 | 131.7 (39.8) | 124.2 (106.1–150.6) | 81.3–239.7 |
| | Last*, n=24 | 170.4 (46.7) | 159.8 (146.0–206.2) | 78.2–253.2 |

Note: Where a wound was observed exactly two times the measures are summarised in the 'Second' rather than 'Last' visit column. *'Last visit' refers to the visit where final NIRS assessments were performed. Note: First visit=day 0/baseline; second visit=day 2–9; last visit=day 7–70 (excludes visit where wound healed)

**Table 11.** Number of wounds (n=23)

| Number of wounds | n (%) |
|---|---|
| 1 | 20 (87) |
| 2 | 1 (4.3) |
| 3 | 1 (4.3) |
| 8 | 1 (4.3) |

with an average follow-up of 28 days per wound. These results are highly consistent with, and in some ways superior to, those reported in previous studies evaluating the efficacy of NPWT on complex wounds.

Several meta-analyses and systematic reviews have documented significant reductions in wound area under NPWT, although these vary according to aetiology and device type. For example, the Cochrane reviews concluded that NPWT can accelerate healing in post-surgical wounds and diabetic foot ulcers, although methodological limitations were identified in many included studies.[32,20,7,8] The present study overcomes these limitations through a structured, prospective approach and standardised longitudinal follow-up.

The results of this analysis reinforce the clinical value of negative pressure with real-time monitoring of physiological parameters. The NPWT system integrates advanced technology to modulate the wound environment more precisely than traditional systems, which could explain the higher closure rate observed.

Unlike previous studies that focused exclusively on structural outcomes (e.g., area, volume and closure time), the present study incorporates physiological parameters measured by NIRS (Hb, $HbO_2$, $StO_2$ and THb), adding a functional dimension that has not been widely documented in the literature. This methodological innovation enables observation of the morphological contraction of wounds and interpretation of the changes in deep tissue oxygenation during treatment.[31,46]

Compared to studies that reported a significant reduction in volume in wounds treated with standard NPWT but with scarce documentation of physiological parameters,[52] the data presented in the current study show greater structural efficiency and a measurable improvement in perfusion from both functional and clinical perspectives.

## Clinical relevance of near-infrared evaluation of therapeutic efficacy

The results demonstrated a progressive increase in $StO_2$, which rose from an average of 60.1% at baseline to 80.2% at the last visit where $StO_2$ was assessed ($P$<0.001, mixed-effects model). At baseline, several wounds presented $StO_2$ values in the hypoxic range (<60%), as the overall mean was 60.0%. By the end of treatment, most wounds (approximately 75%) were within acceptable, good or excellent perfusion ranges (>60%). In the literature, $StO_2$ values above 75% are associated with a favourable prognosis for wound closure.[53]

On a clinical level, the possibility of measuring parameters such as Hb, $HbO_2$ and THb offers additional advantages. In this study, the progressive decrease in Hb (mean daily improvement of 0.64%; $P$<0.01) suggests a reduction in local hypoxia, while the sustained increases in $HbO_2$ ($P$<0.001) and THb ($P$<0.001) reflect enhanced tissue oxygen delivery and perfusion. Together with the rise in $StO_2$, these changes indicate a more favourable environment for angiogenesis, cell proliferation and extracellular-matrix synthesis, ultimately supporting progression toward wound closure.[46,54]

From a medical practice perspective, the use of NIRS can have multiple applications. It allows real-time monitoring of the physiological response to treatment, which is particularly useful in patients with hard-to-heal wounds or vascular risk factors. This analytical technique provides an objective basis for adjusting the intensity, frequency or modality of NPWT, facilitating more dynamic and personalised medicine. It improves communication with the patient and the multidisciplinary team by providing visual and quantifiable indicators of clinical progress, promoting therapeutic adherence. The use of NIRS enriches the characterisation of clinical response and represents an early and quantifiable marker of therapeutic efficacy. Its incorporation into clinical routines can revolutionise the haemoglobin approach to advanced wound management, expanding diagnostic, predictive and real-time monitoring capabilities.[47,54,55]

This study introduces the conceptual framework of smart pressure, which represents an innovation in NPWT by linking therapeutic action with real-time monitoring. While originally conceptual, its value lies in providing a paradigm that can be adapted to different clinical realities, including systems with limited resources.

## Therapeutic personalisation based on healing phases and structural response

The findings of this study provide clinical evidence on the potential for personalising NPWT by adjusting pressure parameters and adjuvant combinations according to the healing phase and structural evolution of the wound (*Figure 2*). Although NIRS was used in this study to quantify physiological changes, the most robust data emerged from the standardised follow-up of structural clinical parameters, such as reductions in area, volume and depth, as well as changes in type of tissue in the wound bed and exudate. All adjuvant therapies, including antimicrobial (e.g., silver) dressings, were applied only after individual assessment and when clinically indicated, in alignment with international antimicrobial stewardship guidance, while mechanical debridement was performed whenever feasible.

### Accelerated and adaptable reduction according to healing phase

The average reduction in wound area was 93%, with a 41% reduction achieved within up to 9 days and an overall wound closure rate of 73%. The successful and rapid reduction in wound area can be attributed to the strategic therapeutic adjustments that were used, including the following:

- Initial use of continuous pressure (125 mmHg), implemented during phases with high exudate and in wounds that had undergone debridement of devitalised tissue, ensuring NPWT was only applied on viable wound beds with controlled residual slough
- Transition to variable intermittent modes (125/60 mmHg or 100/60 mmHg) during the active granulation and epithelialisation phases
- Combination with adjuvant strategies—including anti-microbial dressings, collagen-based dressings or CAMPs, as well as enzymatic, osmotic and autolytic debridement—depending on the condition of the wound bed and tissue evolution, as described in the results section and here interpreted as part of the structure-guided NPWT model, illustrating the role of these adjuvant strategies in therapeutic personalisation.

This sequential approach based on pathophysiology allowed treatment to be adapted dynamically, without the need for aggressive surgical changes or significant complications, achieving closure in 3–6 weeks, even in patients with major comorbidities, such as type 2 diabetes, obesity or arterial insufficiency.

## Personalised therapy without advanced devices

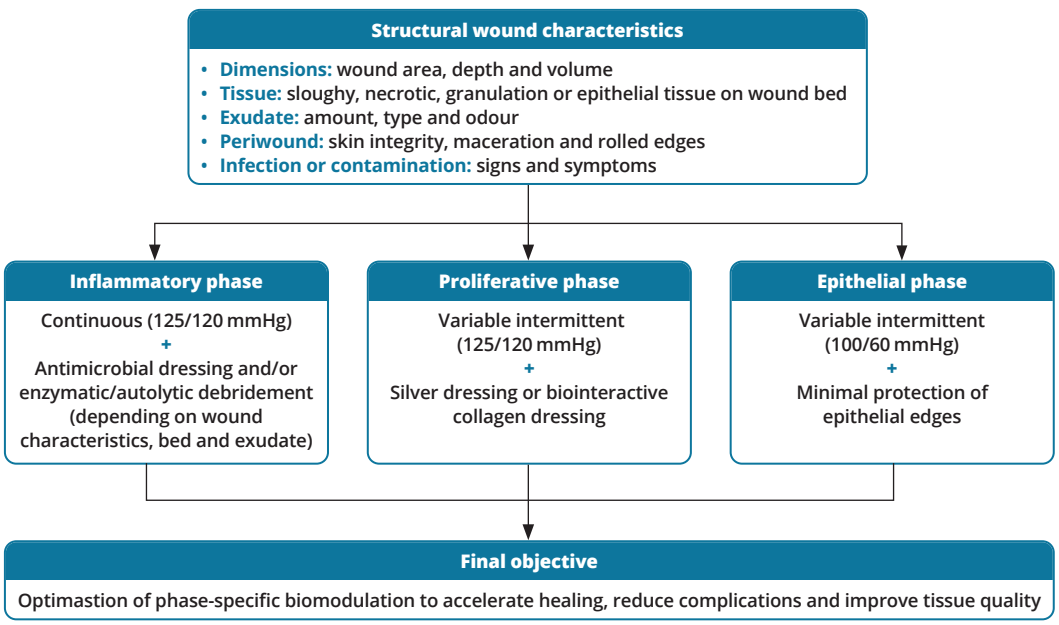
Although NIRS helped to validate some of these physiological changes (e.g., improved oxygenation and perfusion), the true clinical applicability lies in professionals being guided by traditional structural parameters, such as wound size, tissue type on the wound bed, wound edges, exudate levels and periwound skin condition, with the requirement of a structured follow-up. This section reflects one of the main innovations of the present study: to the author's knowledge, no previous publications have systematically described the concept of structure-guided NPWT as a model for clinical biomodulation without advanced monitoring devices. Rather, this proposal represents a paradigm shift derived from clinical observation, aligned with international consensus[4,30,46,50] documents that highlight the central role of structured clinical assessment in wound management. In this sense, the approach represents a practical framework for wound biomodulation, with applicability even in resource-limited clinical settings.

## Indirect comparison with other negative-pressure systems

Studies investigating the application of NPWT in acute and chronic wounds typically report closures in 6–8 weeks, with area reductions between 30–70%.[21,22] In contrast, the results of the present analysis with the NPWT system show faster closure (in 3–6 weeks) and more efficient progression between phases of healing, as evidenced by the rapid transition from non-advancing to advancing wound edges and resolution of slough by the final visits (*Table 7*).

Only one patient presented a transient periwound allergic reaction to adhesive tape, which resolved without sequelae. Importantly, the absence of further perilesional complications and the favourable wound progression were facilitated by the programming flexibility of the NPWT system, which allows pressure and therapeutic modes to

**Figure 2.** Algorithm for personalised negative pressure wound therapy (NPWT) by phase of wound healing




Note: Instructions for use must be consulted when using combined treatments. The therapeutic combinations and sequence shown are consistent with current international consensus documents (EWMA, Wounds International, FDA Guidance, 2024) that recognise NPWT as a complementary tool for wound bed preparation when applied over non-adherent, viable or partially devitalised tissue in combination with appropriate debridement techniques (autolytic, enzymatic, osmotic or surfactant-based). These practices reflect evidence-based clinical use within approved safety parameters. The NPWT system used in this study is not yet cleared for use with biointeractive collagen dressings.

be adapted based on the progress observed, in addition to maintaining a stable closed environment and easy integration with other therapies.

## Personalising treatments based on healing phase and structural response

A key takeaway of this present study is that NPWT can be customized in a safe, efficient and measurable way, guided by observable structural clinical parameters, without the need for advanced modalities such as NIRS. Although NIRS provided an objective physiological quantification for this study, the structural changes (wound size, tissue types, edges and exudate) were sufficient to adjust therapies dynamically and strategically throughout the healing process.

The results of this cohort show that the modulation of pressure—in intensity and mode of application—according to the healing phase (inflammatory, proliferative or epithelial) produced an accelerated and consistent response. These findings are consistent with previous experimental and clinical studies demonstrating improved perfusion and granulation under continuous NPWT during inflammatory phases;[2] the stimulatory effect of intermittent pressure on angiogenesis and tissue reorganisation;[56] and the clinical applicability of adapting NPWT parameters according to tissue response in real-world settings.[9] Together, these studies support the proposal that observable structural changes are sufficient to guide safe and effective therapeutic personalisation, even without advanced devices such as NIRS.

The combined use of NPWT with other complementary therapeutic modalities (in alignment with product instructions for use) enabled optimisation of the therapy and clinical outcomes. These principles coincide with the Tissue, Inflammation, Moisture, Edge (TIME) clinical decision support tool.[57] This approach represents a transition from a static model, in which NPWT is prescribed in a standard way, to an advanced, adaptive therapy focused on the patient's actual tissue evolution. This approach reduces treatment time, exposure to risks arising from wound stagnation and unnecessary use of materials or premature dressing changes. This also supports accurate clinical decision-making without relying on expensive or unavailable technology.

The programmable versatility of the NPWT system, coupled with its compatibility with adjuvant therapies, translates into an effective tool for therapeutic personalisation based on objective clinical criteria. Although this study was conducted in a specialised wound care centre, the portability and design of the device allow its application in diverse clinical contexts (including outpatient clinics, hospital wards and even home care), broadening its practical relevance and supporting its use beyond specialised environments.[41,45,46] This lays the foundation for developing structured protocols for pressure adjustment and therapeutic combinations according to the healing phase, applicable both in high-complexity centres and in general clinical practice.

The results of the present observational study therefore support the adoption of a structure-guided NPWT approach (*Box 2*).

### Box 2. Definition of structure-guided negative pressure wound therapy (NPWT)

**Definition:** Structure-guided negative pressure NPWT is a clinical model of progressive biomodulation and phase-specific therapeutic personalisation, in which decisions are based on systematic structural assessment of the wound—including dimensions, depth, exudate, tissue types and morphological evolution—without requiring advanced quantification technologies.

**Applicability:** This model has been designed for clinical implementation in diverse scenarios, from outpatient centres to hospital units, as it has the capacity for adaptation to environments with limited technological resources.

**Objective:** Structure guided NPWT aims to provide a structured and reproducible strategy to personalise NPWT treatment in real time, optimising clinical results based on the observable pathophysiology of the wound.

**Promoting evidence-based precision medicine:** This approach translates the principles of precision medicine to wound care through a visual and structural clinical language, turning direct observation into an active therapeutic tool.

## Limitations

This study has limitations that should be considered when interpreting the results. The observational case-series design without a parallel control group restricts causal inference and precludes direct comparison with other NPWT systems. The cohort size was modest and included wounds of varying aetiologies and anatomical sites, which may have introduced heterogeneity; however, this diversity also reflects real-world clinical practice and enhances the external relevance of the findings. Follow-up duration varied across patients (7–70 days), potentially influencing the timing of wound closure and perfusion changes, yet this variability offers insight into the performance of NPWT under routine clinical conditions. Periwound complications were not systematically captured in the statistical dataset, although only one minor adverse event was documented in the clinical cohort. Finally, the use of NIRS as a monitoring tool, while innovative, warrants further validation in larger populations to standardise thresholds and optimise its predictive value.

Additionally, in one case (*Appendix 1, Case 4*), NIRS data were lost due to a system update failure. While this represented a minor limitation in data completeness, it did not compromise the clinical follow-up or structural outcome assessment. This incident underscores the importance of ensuring technological interoperability and data integrity when incorporating advanced monitoring systems into clinical research.

Despite these limitations, this analysis provides novel and clinically meaningful data linking structural wound improvement with measurable physiological changes under NPWT. The consistency of these trends across multiple parameters supports the biological plausibility of

NPWT-induced tissue optimisation. Importantly, the real-world observational design strengthens the external validity of the findings by reflecting routine clinical practice.[6] Future prospective, multicentre studies with larger cohorts and comparator groups are warranted to confirm these findings, refine patient selection and further explore the role of NIRS as a surrogate endpoint in wound-care research.

## Conclusions and recommendations

### Conclusions

This prospective, real-world observational study demonstrated that the NPWT system is clinically effective and feasible for the treatment of complex wounds of multiple aetiologies and anatomical locations (*Box 3*). Through the analysis of 33 wounds in 23 patients, an average reduction of 93% in wound area was documented, with a total clinical closure rate of 73% in an average follow-up period of 28 days. Consistent reductions in wound volume reflected the overall structural improvement observed.

The quantified structural evolution demonstrated a progressive and sustained response across subgroups, with reductions already evident in the first week of treatment and consolidation of closure typically within 3–6 weeks. Improvements were achieved even in patients with multiple risk factors, such as diabetes, obesity, peripheral vascular disease and complex surgical histories.

Therapeutic management was not uniform but adapted to the predominant healing phase in each case, using continuous or intermittent pressure modes and combining adjuvant therapies—such as antimicrobial dressings, collagenase, collagen-based dressings, hydrogels or CAMPs—according to clinical need. This phase-specific intervention strategy was key to modulating tissue evolution, optimising the healing environment and avoiding stagnation.

Although NIRS was used as a complementary tool to measure physiological parameters, the effectiveness of

**Box 3. Glossary of terms related to structure-guided negative pressure wound therapy (NPWT)**

**Angiogenesis:** Formation of new blood vessels induced by negative pressure through mechanical stress and release of VEGF and IL-8[13,14]

**Biomodulation:** Active modulation of the biological wound environment through cellular, biochemical and structural mechanisms that promote orderly and physiologically viable healing[2,12]

**Clinical closure:** Complete epithelialisation of a wound, achieved after granulation processes, tissue reorganisation and control of the microenvironment

**Continuous pressure:** NPWT mode used in inflammatory phases or with high exudate to promote control of the microenvironment[2]

**Deoxygenated haemoglobin (Hb):** Physiological indicator of hypoxia[10]

**Glutathione:** key antioxidant involved in cellular defence against oxidative stress[26]

**Interleukin-8 (Il-8):** Proinflammatory interleukin that promotes angiogenesis and cell migration in wounds treated with NPWT[14]

**Intermittent pressure:** NPWT application mode that alternates pressure cycles, favouring granulation and tissue reorganisation[3]

**Matrix metalloproteinases (MMPs):** Degradative enzymes reduced by the action of NPWT in removing exudate and controlling pH[4,12]

**Microdeformation:** A mechanical stimulus generated by NPWT that induces cell cytoskeleton reorganisation, cell migration and extracellular-matrix synthesis[2,4]

**Near-infrared spectroscopy (NIRS):** Non-invasive technology that allows tissue oxygenation and perfusion to be quantified in real time using near-infrared light[9]

**Nitro tyrosine:** Marker of protein oxidation and nitrosative stress[26]

**Oxygenated haemoglobin ($HbO_2$):** Physiological indicator of good tissue perfusion[10]

**Precision wound medicine:** Clinical approach that adapts therapeutic strategies based on structural, physiological and patient-specific characteristics, aiming to optimise outcomes in complex wounds[28]

**Real-world evidence:** Data derived from clinical practice outside the controlled environment of randomised trials, used to complement efficacy findings with insights on effectiveness and feasibility[6]

**Smart pressure:** Conceptual framework, introduced in this article, to describe a therapeutic approach in which NPWT acts and monitors simultaneously, allowing individualised adjustments; it integrates structural wound evaluation with real-time physiological biofeedback (e.g., NIRS), aligning with the principles of precision wound medicine and responsive therapy

**Structure-guided NPWT:** Clinical model, introduced in this article, of progressive biomodulation and phase-specific therapeutic personalisation, based on systematic morphological evaluation of the wound (wound size, tissue types, edges and exudate) without the need for advanced quantification technologies

**Thiobarbituric acid reactive substances:** Marker of lipid peroxidation and oxidative stress[26]

**Tissue oxygen saturation ($StO_2$):** Physiological indicator of functional level of oxygenation[10]

**Total antioxidant capacity:** Global marker of antioxidant activity in tissues[26]

**Total haemoglobin (THb):** Physiological indicator of functional vascular volume and microvascular perfusion[10]

**Vascular endothelial growth factor (VEGF):** Growth factor key to angiogenesis induced by negative pressure and mechanical stress[13,14]

the NPWT system and its therapeutic adjustments were essentially guided by structural clinical observation. This strengthens the concept of structure-guided NPWT as a reproducible strategy that can be applied both in specialised centres and in clinical environments with limited access to advanced monitoring technologies. Taken together, these findings support the use of the NPWT system as a highly precise and adaptable therapeutic option, capable of inducing effective tissue biomodulation, accelerating healing times and reducing the care burden associated with complex wounds.

## Clinical implications

The main clinical implication of this study is that the personalisation of NPWT based on structural wound characteristics provides an objective framework for guiding treatment and appeared to accelerate the wound closure process. Although NIRS was used in this study as a complementary validation tool, the structure-guided NPWT model was intentionally designed to be reproducible even without access to advanced monitoring. This ensures that clinical adjustments can be safely guided by observable structural parameters (wound size, tissue types, edges and exudate), allowing the model to be emulated across diverse clinical contexts while maintaining an evidence-based foundation.

By dynamically adapting therapy—such as alternating between continuous and intermittent pressure modes depending on wound bed evolution—tissue stimulation could be optimised and sustained healing supported (*Figure 3*). The cohort demonstrated progressive closure trajectories within 3–6 weeks of follow-up, including patients with multiple comorbidities, underscoring the adaptability of this approach.

From an operational standpoint, the NPWT system demonstrated advantages in adaptability across wound sizes and anatomical sites, including difficult-to-seal areas such as the sacrum, buttocks and lower extremities. Its adjustable negative pressure range (60–125 mmHg) facilitates individualised therapy within physiologically safe parameters. Compatibility with adjuvant therapies was also observed, without apparent compromise in system function.

These findings highlight the clinical flexibility and potential cost-effectiveness of the NPWT system by reducing healing times, limiting unnecessary interventions and mitigating complications that prolong care. This study therefore provides a practical and evidence-based perspective on NPWT personalisation, with applicability in specialised wound centres, outpatient clinics, intermediate care units and public health systems with limited access to advanced technology.[8]

## Recommendations for clinical practice

Considering the results obtained, several recommendations can be highlighted to optimise and expand the clinical impact of this therapeutic strategy. Institutional protocols should be developed in alignment with the phases of wound healing, where NPWT mode and pressure are dynamically adjusted according to the

**Figure 3.** Therapeutic map for personalisation of negative pressure wound therapy (NPWT) according to structural evolution

**1. Initial assessment** (visual diagnosis)

- **Aetiology:** pressure, neuropathic, diabetic, surgical, etc
- **Dimensions:** wound area, depth and volume
- **Tissue:** sloughy, necrotic, granulation or epithelial tissue on wound bed
- **Exudate:** amount, type and odour
- **Periwound:** skin integrity, maceration, rolled edges
- **Infection or contamination:** signs and symptoms

**3. Rapid therapeutic decision algorithm** (traffic light style)

- **Stop:** Excessive exudate and adherent devitalised tissue —> NPWT + debridement
- **Caution:** Stagnant granulation >7 days—> change pressure mode or adjuvant therapies
- **Follow:** Reduction >30% in 7 days —> maintain protocol, adjust pressures if epithelialised

**2. Predominant healing phase** (simplified visual scale)

**Inflammatory phase (debridement)**
- Continuous pressure at 125 mmHg
- Combination with antimicrobial dressings or enzymatic/autolytic debridement
- Review every 2–3 days

**Proliferative phase (active granulation)**
- Intermittent pressure at 125/60–100/60 mmHg
- Biointeractive collagen dressings or cross-linked foams
- Weekly evaluation of volumetric evolution

**Epithelial phase (remodeling)**
- NPWT phaseout
- Conventional or advanced complementary therapies
- Regular photographs and definitive healing plan

**Model advantages**

- Does not rely on expensive sensors
- Supported by observable physiology and morphology
- Reproducible in multiple clinical settings
- Facilitates real-time decisions

**Structured clinical record sheet** (practical checklist)

- ☐ Area (cm²) and depth (cm)
- ☐ Dressing type
- ☐ Exudate (low/moderate/high)
- ☐ NPWT pressure and mode
- ☐ Applied combination therapies
- ☐ Photo attached
- ☐ Response to treatment (e.g., % reduction vs previous visit)

Note: Instructions for use must be consulted when using combined treatments.

Source: Original figure elaborated by author

clinical signs of each phase (inflammatory, proliferative or epithelial).

In addition, the incorporation of visual algorithms and structured monitoring tools, such as serial photography, wound evolution curves and morphological scales, is recommended to facilitate timely decision-making. These resources should be simple, accessible and standardisable, enabling their adoption across all levels of care, including primary care. Clinical staff training in the dynamic interpretation of the wound bed and in the rational use of combined therapies, in accordance with the product's instructions for use (e.g., collagenase, antimicrobials, biointeractive collagen dressings), is also essential to allow treatment adjustment based on structural evolution and reduce dependence on advanced technological quantification.

Finally, structure-guided NPWT should be formalised as an operational model for clinics, hospitals and home-care programmes, incorporating this strategy into institutional policies as a precision medicine approach to wound care. Its progressive inclusion in clinical guidelines and regulatory frameworks would reinforce its value as a paradigm of personalised intervention in complex wounds. Standardisation of this strategy has the potential to optimise resources, shorten healing times and improve outcomes in a reproducible and cost-effective manner.

## Future research

The findings of this study provide preliminary real-world evidence on the structural and physiological efficacy of next-generation NPWT, while also highlighting opportunities for future investigation. Further research should aim to validate the structure-guided NPWT model in larger, prospective, multicentre cohorts to strengthen external validity and to confirm the reproducibility of these results across diverse healthcare systems. There is also scope for the development and testing of clinical algorithms based on structural parameters, which could be implemented even in resource-limited settings as pragmatic decision-support tools.

In addition, integration of NIRS and other physiological monitoring methods with advanced analytics, including artificial intelligence, may help to correlate structural wound trajectories with real-time therapeutic optimisation. This approach could generate predictive models that support precision wound care and patient-specific treatment pathways. Overall, the present study establishes a foundation for future publications, multicentre collaborations and institutional proposals aimed at advancing personalised strategies in wound management.

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# Appendix 1: case studies

## Case study 1

### Presentation

A 48-year-old woman presented with multiple open dehisced surgical wounds following a complex procedure (*Figure 4*). The wounds were located in five regions:

1 Under the right nipple
2 Under the right breast
3 Under the left nipple
4 Under the left breast
5 Pelvic area (a–d)

Initial assessment on presentation revealed extensive tissue damage across all sites, with extensive coverage by slough (up to 100%) and high exudate. NPWT was initiated as an adjuvant to phased debridement (autolytic/enzymatic or osmotic as indicated) with serial mechanical debridement at each dressing change, protection of sensitive structures using a non-adherent interface and strict exclusion of spreading or systemic infection. The wound edges were largely non-advancing, and the periwound skin showed erythema and oedema, compounded by allergic reactions to adhesive tape. NIRS indicated severely compromised tissue oxygenation, with $StO_2$ as low as 4% in the first wound (under right nipple).

### Intervention

NPWT was initiated using variable intermittent pressure settings (range 100–120/60–80 mmHg, 10/2 minutes). The patient attended the clinic nine times over the span of 1 month. Therapy was briefly discontinued on the second visit (day 7) due to allergic skin reactions to tape in the breast but resumed on day 9 following resolution of the reaction. NIRS was used throughout to monitor tissue perfusion and oxygenation.

### Outcomes

The patient showed significant improvement across all wound sites. All wounds reduced significantly in size, with seven of eight wounds achieving full closure by day 21 of treatment. Wound tissue compositions also drastically improved, with wounds no. 2–5 achieving 100% epithelialisation and wound no. 1 progressing from 15% granulation tissue and 85% slough to 50% granulation tissue, 15% slough and 35% epithelial tissue. Exudate volume decreased from 300 ml to 20 ml over the course of treatment, with consistency shifting from thick purulent to thin serosanguineous.

NIRS metrics demonstrated improvements in wound tissue from day 1 to month 1 (*Table 12*), with significant increases in $StO_2$ (e.g., 87% increase in wound no. 1), overall decrease in Hb indicating reduced hypoxia, as well as increases in $HbO_2$ and tHb, reflecting improved oxygen delivery and vascularisation.

By 1 month, all wounds except one (wound no. 1) had fully closed, and tissue oxygenation had normalised.

## Case study 2

### Presentation

A 54-year-old man presented with a dehisced surgical wound at the distal phalanx of the third finger on the right hand (*Figure 5*). The wound followed a re-graft procedure performed by a hand surgeon. Initial assessment revealed a wound measuring 2.5×1.5 cm, with non-qualifying depth, coverage by 100% slough and perilesional oedema. NPWT was applied strictly as an adjuvant to phased debridement, with serial mechanical debridement at each dressing change complemented by autolytic/enzymatic methods where indicated. The wound edge showed no advancement, and NIRS indicated severely compromised tissue oxygenation ($StO_2$ 1%).

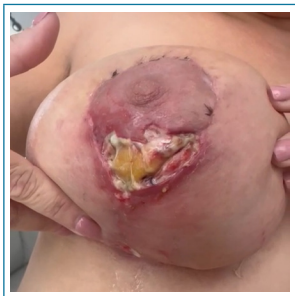
### Intervention

NPWT was initiated at a continuous pressure of 125 mmHg. Over subsequent visits, the therapy mode was adjusted to variable intermittent settings (100–125/60 mmHg, 10/5 minutes) in response to wound progression. NIRS was used to monitor tissue perfusion and oxygenation. The wound was evaluated across five visits over 13 days, with assessments of wound size, tissue types, edges and exudate.

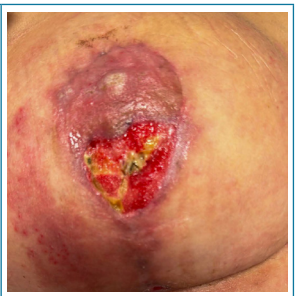
### Outcomes

The patient demonstrated rapid and sustained wound healing. Wound 1 reduced from 2.5×1.5 cm to 0.2×0.2 cm over 13 days. Tissue composition transitioned from 100%

**Figure 4.** Case study 1

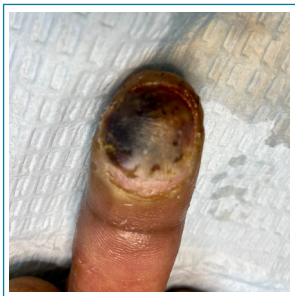


Baseline

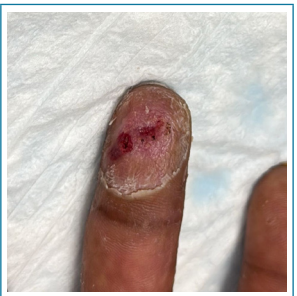


Month 1

**Figure 5.** Case study 2



Baseline



Day 13

slough to 90% epithelial tissue and 10% granulation tissue. The wound edge progressed from non-advancing to complete advancement, supporting closure, and exudate was recorded as very low.

NIRS results demonstrated a significant improvement in $StO_2$ (increasing from 1% to 87%) and a corresponding decrease in Hb, indicating reduced hypoxia. $HbO_2$ increased by 194 µM and THb increased by 132.2 µM, suggesting improved oxygen delivery and revascularisation (*Table 12*).

NPWT was discontinued on day 13 due to near-complete wound closure and optimal tissue regeneration. The patient experienced a fast and successful recovery with NPWT, showing significant wound reduction, complete elimination of devitalised tissue and a notable increase in oxygenation and tissue perfusion.

## Case study 3
### Presentation
A 46-year-old man presented with a traumatic wound to the anterior aspect of the right leg following a motor-vehicle accident (*Figure 6*). His medical history included diabetes mellitus and chronic venous insufficiency, both contributing to impaired wound healing. Initial assessment revealed a wound measuring 6×2.5×1.5 cm, with tunnelling and undermining at both the 12 o'clock and 6 o'clock positions. The wound bed contained 50% slough and 50% granulation tissue, with a high volume of clear exudate (50 ml). The wound edge was non-advancing and periwound skin showed perilesional oedema.

### Intervention
NPWT was initiated at a continuous pressure of 125 mmHg. On day 3, the therapy was adjusted to variable intermittent settings (125/60 mmHg, 10/5 minutes), then reduced to 100/60 mmHg from day 9 onward as the wound progressed. NIRS was used to monitor tissue oxygenation and haemoglobin dynamics throughout the treatment period. Over six visits spanning 1 month, the wound was evaluated for size, tissue types, edges and exudate.

### Outcomes
The patient demonstrated consistent and measurable improvement throughout the treatment period. Wound dimensions reduced from 6×2.5×1.5 cm to complete closure in 1 month. Tunnelling and undermining at both 12 o'clock and 6 o'clock positions resolved entirely by day 20. Tissue composition transitioned from 50% slough to 100% epithelial tissue. Exudate volume decreased from 50 ml to 20 ml within 3 days of treatment, after which it was no longer measurable. The wound edge advanced progressively until wound closure, and the periwound skin normalised, with oedema resolving by the third visit.

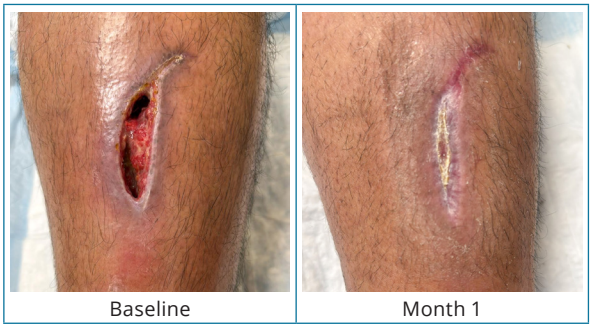
NIRS demonstrated significant improvements in $StO_2$, $HbO_2$ and THb, as well as reduction in Hb. These improvements reflect enhanced oxygen delivery, reduced hypoxia and increased vascularisation (*Table 12*).

## Case study 4
### Presentation
A 71-year-old woman presented with wound dehiscence following a replacement of the right knee (*Figure 7*). Her medical history included hypertension, obesity and type 2 diabetes, all contributing to delayed wound healing. The initial assessment revealed a wound measuring 7×1×0.4 cm with no advancing edge and perilesional oedema. The wound bed was composed of 80% slough and 20% granulation tissue, with moderate levels of clear exudate. NIRS indicated poor tissue oxygenation and perfusion.

### Intervention
NPWT was initiated at a continuous pressure of 125 mmHg. On subsequent visits, the therapy was adjusted to variable intermittent settings: 125/60 mmHg on day 4 and 100/60 mmHg on days 14–18, both at 10/5 minutes. NPWT was discontinued on day 25, following near-complete wound closure. NIRS was conducted in this case; however, due to a technical failure during a system software update, the recorded data were irreversibly lost. This constituted an isolated incident that limited the completeness of the dataset for this particular case, although structural clinical outcomes were fully documented and unaffected.

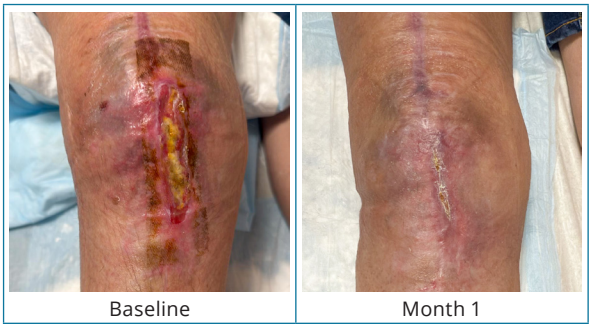
### Outcomes
The patient demonstrated steady and complete wound healing by the end of the treatment period (1 month). Wound dimensions reduced from 7×1×0.4 cm to full closure after 1 month of treatment. Tissue composition transitioned from 80% slough to 100% epithelial tissue. The wound edge progressed from non-advancing to fully

**Figure 6.** Case study 3



Baseline | Month 1

**Figure 7.** Case study 4



Baseline | Month 1

advancing, supporting closure. Periwound skin improved from oedematous to intact without complications, with only minor maceration noted before closure. Exudate levels decreased from moderate to low, with consistency remaining clear throughout.

## Case study 5
### Presentation
A 51-year-old woman presented with an open surgical wound on the right inner thigh following a post-infection dehiscence (*Figure 8*). The wound measured 5×4×3 cm at initial assessment, with 80% granulation tissue and 20% yellow slough. The wound edge was non-advancing, and the periwound skin showed perilesional oedema. The exudate was thick and high in volume.

### Intervention
NPWT was initiated at 150 mmHg in continuous mode, later adjusted to 125 mmHg on day 24, then to variable intermittent settings (100/60 mmHg, 10/5 minutes) for days 38–53. Over seven visits spanning 53 days, wound progression was tracked through dimensional changes, tissue composition and NIRS metrics.

### Outcomes
The wound showed a favourable healing trajectory, characterised by reduced wound size, with dimension reducing from 5×4×3 cm to full closure by day 53. Tissue composition transitioned from granulation tissue and slough to 100% epithelialisation. Exudate volume decreased from 200 ml on day 4 to 30 ml on day 31 and to non-measurable levels by the end of treatment.

The patient underwent NIRS at first visit and on day 38. The results demonstrated significant improvements in tissue oxygenation and perfusion parameters (*Table 12*).

## Case study 6
### Presentation
A 70-year-old man with a history of type 2 diabetes and hypertension presented with a hard-to-heal open surgical wound at the Achilles' heel (*Figure 9*). The wound measured 1.5×0.5×0.7 cm at presentation, with 100% granulation tissue and low exudate. The wound edge was initially non-advancing, and the periwound skin showed oedema.

### Intervention
NPWT was initiated at 125 mmHg continuous, then adjusted to variable intermittent mode (100/60 mmHg, 10/5 minutes) on days 7, 10 and 17, with a temporary return to 125 mmHg continuous on day 14. Therapy was discontinued after 19 days due to perilesional erythema. NIRS was performed to assess tissue oxygenation.

### Outcomes
The wound showed positive healing trends characterised by significant size reduction, progression of wound edges, maturation of the wound bed from granulation to epithelial tissue and improved tissue oxygenation. The wound size reduced from 1.5×0.5×0.7 cm to 0.5×0.2×0.2 cm over 17 days. Tissue composition progressed from 100% granulation tissue to 50% epithelial tissue and 50% granulation tissue by day 19. Exudate remained low throughout treatment and transitioned from thick to clear.

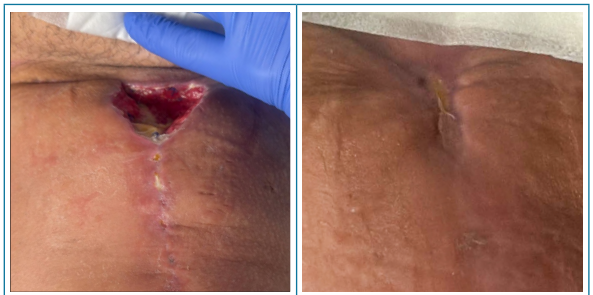
Despite a decrease in both $HbO_2$ and tHb levels, the observed increase in $StO_2$ and reduction in Hb suggested an improvement in microvascular function and oxygen delivery efficiency (*Table 12*). This reflects a positive biomodulation response and a favourable trend toward wound healing.

The integration of NPWT and NIRS provided a comprehensive view of tissue response, reinforcing the role of NPWT as an effective intervention in complex open surgical wounds, particularly those in anatomically challenging areas such as the Achilles' heel. Early detection of perilesional erythema allowed timely discontinuation of therapy, emphasising the importance of close clinical monitoring during advanced wound treatments.

## Case study 7
### Presentation
A 45-year-old man with type 1 diabetes and renal failure presented with a neuropathic wound on the plantar surface of the right foot (*Figure 10*). Initial wound size was 1.5×1.5×1 cm, with 100% slough and high exudate. Periwound skin showed callous formation, oedema and erythema. The wound edge was non-advancing.

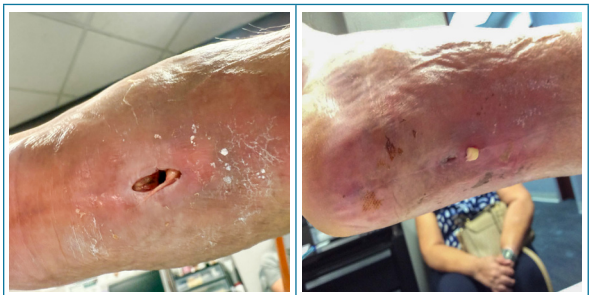
### Intervention
NPWT was applied continuously at 125 mmHg throughout

**Figure 8.** Case study 5



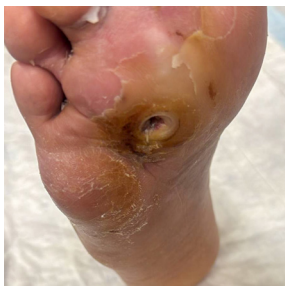
Baseline | Day 38

**Figure 9.** Case study 6

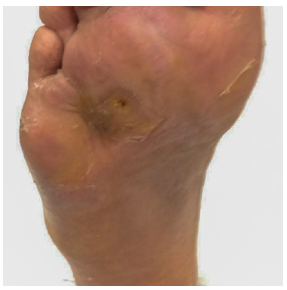


Baseline | Day 14

**Figure 10.** Case study 7

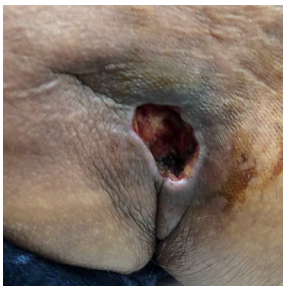


Baseline

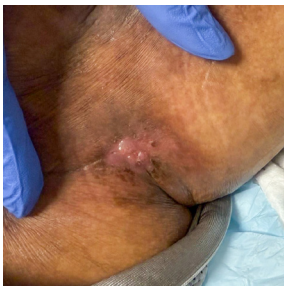


Day 17

**Figure 11.** Case study 8



Baseline



Day 42

**Table 12.** Change in physiological metrics from beginning to end of treatment

| Case, wound | Endpoint | $StO_2$ (%) | Hb (µM) | $HbO_2$ (µM) | tHb (µM) |
|---|---|---|---|---|---|
| Case 1, wound 1 | Month 1 | 87 | -46.8 | 183.2 | 136.47 |
| Case 1, wound 2 | Month 1 | 23 | -6.9 | 76.5 | 69.6 |
| Case 1, wound 3 | Month 1 | 29 | 19.7 | 62.5 | 42.9 |
| Case 1, wound 4 | Month 1 | 14 | -2.8 | 62.1 | 59.4 |
| Case 1, wound 5 | Month 1 | 14 | -8.3 | 54.1 | 45.7 |
| Case 2 | Day 13 | 86 | -61.77 | 194.0 | 132.2 |
| Case 3 | Month 1 | 6 | −19.7 | 74.1 | 54.5 |
| Case 5 | Day 38 | 13 | −17.6 | 31.5 | 13.8 |
| Case 6 | Day 14 | 7 | -5.2 | -6.7 | -11.0 |
| Case 7 | Day 17 | 5 | -18.3 | -33.6 | -51.9 |
| Case 8 | Day 42 | 6 | -2.0 | 33.2 | 31.2 |

treatment (across six visits spanning 24 days). NIRS monitoring was performed across three visits (days 1, 10 and 17) to assess perfusion and oxygenation. Therapy continued until complete epithelialisation was achieved.

## Outcomes

The wound progressed favourably throughout treatment and closed by day 23. Wound size reduced from 1.5×1.5×1 cm to full closure 23 days after the commencement of treatment. Tissue transitioned from slough to granulation and then to 100% epithelialisation. Exudate volume decreased from high to low after 17 days.

Despite reductions in $HbO_2$ and THb, the increase in $StO_2$ and decrease in Hb suggested improved oxygen utilisation and vascular remodelling (*Table 12*).

# Case study 8

## Presentation

A 64-year-old man presented with a pressure ulcer at the right ischium, complicated by necrotising fasciitis, diabetes mellitus type 2, hypertension and asthma (*Figure 11*). The initial wound size was 2.3×2.5×1.2 cm, with 30% slough and high exudate. The wound edge was non-advancing, and the periwound skin showed oedema.

## Intervention

NPWT began at 125 mmHg continuous until day 7 of treatment, then was adjusted to variable intermittent mode (100/60 mmHg) from days 10–37 (over 13 clinical visits). NIRS was conducted on day 1 and day 42. Therapy was tailored to wound progression, with consistent clinical evaluations.

## Outcomes

The wound showed complete resolution by the end of the treatment period (42 days). Wound size reduced from 2.3×2.5×1.2 cm to full closure by day 42. The tissue progressed from slough to granulation tissue and then to epithelialisation. Exudate volume decreased from high to none.

Improvements in NIRS metrics reflect enhanced perfusion, reduced hypoxia and successful wound closure (*Table 12*).

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