## **FLOWOX**<sup>TM</sup>



Non-invasive solution to improve mobility, heal wounds and prevent amputation



post@dmedical.no dmedical.no

### **D**Medical

We are a significant supplier in the health care market. We provide several different products within the following product categories: hygiene, surgery, waste management and rehabilitative treatment.

### 77

Together we can create a safer, healthier and more hygienic life.

#### **Our Shared Responsibility**

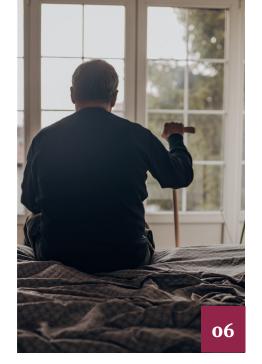
We care about our effect on the environment and the community, therefore we set strict demands to ourselves and how we operate our business. DMedical is a "Miljøfyrtårn" environmentally certified company. Our goal is to continuously work towards preventing pollution from our own operations and the products we supply.

As a member of **Ethical Trade Norway**, we work purposefully to safeguard human and worker rights, as well as society and the environment in our collaboration with our partners. We want to help ensure decent working and environmental conditions throughout the supply chain.

As a member of **"Grønt Punkt Norge"** we follow strict guidelines and instructions for packing and utilizing materials during our transportation.



#### Read more at www.dmedical.no



#### Clinical Background FlowOx™

#### CLINICAL BACKGROUND

FlowOx<sup>™</sup> is recommended for patients who suffer from blood flow deficiencies in the lower limbs.

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The Fontaine Classification





### **Home Treatment**

With FlowOx<sup>™</sup>

#### FLOWOX™

FlowOx<sup>™</sup> is a non-invasive treatment, designed for patients to operate in their own homes.

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#### Clinical Data and Evidence

#### CLINICAL DATA AND EVIDENCE

Through the years, the science behind the mechanisms of action with FlowOx<sup>™</sup> have been carefullly studied. In this brochure we present the key reports and studies.

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### FlowOx<sup>™</sup> is an Intermittent Negative Pressure Therapy

FlowOx<sup>™</sup> is a revolutionary new technology for the treatment of **reduced peripheral circulation.** The technology is based on a tested and gentle intermittent negative pressure technology.

### FLOW**OX**™



A non-invasive, non-sterile medical device, designed for patients to operate in their **own homes.** 

CE Marked (CE 2460)

### Which patients

Can benefit from FlowOx<sup>™</sup>?

#### CLINICAL BACKGROUND

FlowOx<sup>™</sup> is indicated for the treatment of the following conditions in adults over the age of 18:

- **1. Peripheral Arterial Disease** such as intermittent claudication, rest pain or wounds.
- 2. Diabetic and non-diabetic arteriophatic foot- and leg ulcers
- Foot and lower leg ulcers of mixed aetiology associated with immobility such as paraplegia following spinal injury

FLOWOX"





### **Peripheral Arterial Disease (PAD)**

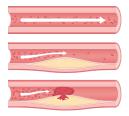
Severe cases of **narrowing** or **blockage** of the **arteries** in the **legs** or lower extremities

#### CLINICAL BACKGROUND

#### Arteriosclerosis

Arteriosclerosis occurs when the blood vessels that carry oxygen and nutrients from the heart to the rest of the body (arteries) become thick and stiff — sometimes restricting blood flow to the organs and tissues. Healthy arteries are flexible and elastic.

This buildup of plaque, also known as atherosclerosis, narrows or blocks blood flow, reducing circulation of blood to the legs, feet, or hands.



Arteriosclerosis is the main cause for PAD. PAD may be asymptomatic, or symptomatic causing intermittent claudication or CLI.

#### **Peripheral Arterial Disease**

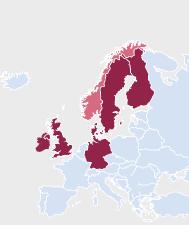
PAD is a common circulatory problem in which narrowed arteries reduce blood flow to the limbs. When developing PAD, the extremities — usually the legs does not receive enough blood flow to keep up with the demand.

#### Intermittent Claudication

Claudication is pain caused by too little blood flow to muscles during exercise. Most often this pain occurs in the legs after walking at a certain pace and for a certain amount of time — depending on the severity of the condition. The pain usually isn't constant, it begins during exercise and ends with rest.

#### **Critical Limb Ischemia (CLI)**

CLI is the advanced stage of PAD, which results from a progressive thickening of an artery's lining (caused by a buildup of plaque). The clinical definition of CLI is rest pain and/or arterial wounds. This is a chronic disease where there is a significant reduction in blood flow to the limbs, which can lead to tissue death, gangrene, and amputation.



#### Registered CLI/PAD Cases in Europe

Norway

CLI	33 000
PAD	88 000

Germany, UK, Sweden, Finland, Denmark

CLI	1 710 000
PAD	12 287 000

**4,000** Surgical procedures per year

**NOK 100 000** Per patient annually

800

Amputations per year

### NOK 500-800 million

Annual amputation cost



### What problems are caused by ischemia?

#### CLINICAL BACKGROUND

**Ischemia** is lack of oxygen and other nutrients, and reduced removal of metabolites, due to reduced blood flow. This condition can cause pain, and lead to unhealing wounds and gangrene.

#### **Reduced quality of life**

Living with ischemia and having a chronically poor peripheral circulation has shown a significant and accelerating negative impact on patients' quality of life.

#### The condition causes

patients to struggle with discomfort, pain and a lack of mobility. This results in an increasing use of pain medication and a limited ability to engage in physical activities.

Additionally, this patient group has limited options for treatment (often limited to palliative care).

#### **Financial challenges**

The financial burden of treating patients with insufficient peripheral microcirculation is extensive and increasing:

The annual cost of treating chronic wounds in home care amounts to NOK 100,000 per patient<sup>1</sup>.

### Approximately 4,000 surgical procedures

(revascularizations) are performed on patients with reduced peripheral blood circulation. The number is increasing by about 5 % per year.<sup>2</sup>



#### More than 800 amputations

are carried out annually in Norway and the cost of this is NOK 500-800 million.<sup>3</sup>

It is expected that the societal cost of reduced macro- and microcirculation will increase significantly with the aging population and the increased prevalence of patients with diabetes.

## What are the effects of reduced macro- and microcirculation?

*Microcirculation* is the blood flow through the smallest arteries in the circulatory system. *Macrocirculation* is the circulation of blood to and from the organs, as distinguished from microcirculation.

Reduced macro- and microcirculation can lead to lack of nutrition, oxygenation, and reduced removal of metabolites from the tissue.

This may cause the following:

- Ischemic pain
- Reduced local immune function and thereby increased risk of infections
- Reduced ability to produce
  collagen and thereby limiting
  the tissue's ability to heal itself.

**Collectively,** this reduces the body's ability to form new blood vessels and its ability to heal wounds.

**Over time,** the condition will become chronic and progressive, increasing the need for long term pain management, wound healing, and palliative care. The condition often deteriorates to a stage where amputation is inevitable.



#### Sources

- 1. Jorunn Hagen Rønsen; UiO 2012: Costs for the treatment of chronic leg ulcers in home nursing.
- 2. Wendt K, et al. BMJ Open 2017;7
- 3. Otivio.





### **The Fontaine Classification**

A system used to categorize the severity of peripheral arterial disease (PAD) based on symptoms.

The most used classifications of lower extremity PAD are **Fontaine** and **Rutherford.** 

#### CLINICAL BACKGROUND

**The Fontaine Classification system** is a widely used method for categorizing the severity of PAD based on the symptoms experienced by individuals. It was first introduced in 1954 by Dr. Paul Fontaine and has since become a valuable tool for healthcare professionals in diagnosing and managing PAD.

**The Classification system includes five stages,** ranging from asymptomatic (Stage I) to severe tissue damage (Stage IV). By identifying the stage of PAD, healthcare providers can determine appropriate treatment options and help improve quality of life for those living with the disease.

**Stage I:** Asymptomatic No symptoms are present, but there may be evidence of PAD on diagnostic tests.

**Stage IIA:** Mild claudication Symptoms include cramping, pain or fatigue in the legs during exercise that improves with rest.

Painfree walking distance > 200 m

#### Stage IIB: Moderate claudication

Symptoms are similar to Stage IIa, but they are more severe and occur with less exercise.

Painfree walking distance < 200 m

**Stage III:** Rest pain Pain occurs in the legs or feet at rest, usually at night, and is relieved by dangling the legs over the side of the bed.

#### Stage IV: Ulceration or gangrene

The most severe stage, with non-healing wounds or gangrene (tissue death) present in the feet or toes.

It is important to note that not all individuals with PAD progress through all stages, and treatment options may vary based on the severity of symptoms.



### **The Treatment Stages of PAD**

Following the Fontaine classification

Grade PAD Fontaine Stages	Standard Treatment	Option to standard treatment	Rationale (FlowOx™ treatment)
Stage I	Diet changes Exercise Quit smoking Secondary preventive drugs		
Stage IIA	Diet changes Exercise Quit smoking Secondary preventive drugs		Patients can start using FlowOx at this stage, as supplement to standard care.
Stage IIB	Diet changes Exercise Quit smoking Secondary preventive drugs Endovascular or open surgical treatment		FlowOx™ is a supplement to standard care. There is a universal scientific consensus that 2/3 patients are unable to attend SET.
Stage III	Diet changes Exercise Quit smoking Secondary preventive drugs Endovascular or open surgical treatment		FlowOx™ is a supplement to standard care. There is a universal scientific consensus that 2/3 patients are unable to attend SET.
Stage IV	Secondary preventive drugs Endovascular or open surgical treatment		Relevant for patients that are not amenable for endovascular or open surgical treatment.
Post Revascularization	Diet changes Exercise Quit smoking Secondary preventive drugs		FlowOx™ is an addition to endovascular treatment when increased risk of restenosis. Supplement after bypass surgery.



### FlowOx<sup>™</sup> THE TECHNOLOGY

- ✓ Passive vascular exercise
- ✓ Increased walking distance
- $\checkmark$  Improved quality of life

### FlowOx<sup>™</sup> is an Intermittent Negative Pressure Therapy

FlowOx<sup>™</sup> is a novel **CE Certified**, **Class IIa Medical Device** which improves blood flow to patients' legs by applying a negative oscillating pressure. It is comfortable, it can be used while patients are at rest and there is no barrier for regular use. It can transiently increase blood flow in lower extremities by about 60% in the small arteries and more than 100% in the capillaries. FlowOx<sup>™</sup> is a non-invasive, non-sterile device enabling patients to treat themselves in their own home. FlowOx<sup>™</sup> is a simple to use treatment alternative for both patients and health care institutions.

#### FlowOx<sup>™</sup> helps to improve the quality of life

for patients with a lifelong treatment plan with a high number of doctors appointments, i.e. PAD patients who suffer from leg pain and wounds.

#### FlowOx<sup>™</sup> help the medical care by

reducing the time and cost spent on PAD patients with a life long treatment plan.





HOME TREATMENT

### **FlowOx**<sup>TM</sup>

#### Enables active home treatment

Otivio has developed FlowOx<sup>™</sup> for patients suffering from the effects of PAD such as leg pain and chronic wounds. Early long-term testing documents increased blood flow, pain reduction, wound healing and amputation prevention.

#### FLOWOX™

#### **Home Treatment**

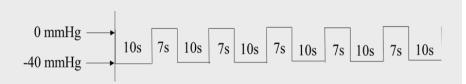
FlowOx<sup>™</sup> is large for a boot, but small for a medical appliance. It is perfectly fine to use at home, and can easily be tidied away if needed. It is also easy to use simply with the press of a button, so no assistance is needed.



#### The Technology

#### Intermittent Negative Pressure (INP)

- Intermittent negative pressure (evacuating 5% of the air, -40mmHg)
- Intermittent suction draws blood to the leg and skin while allowing blood to return during the normal pressure phase (0 mmHg)









HOME TREATMENT

### **FlowOx<sup>™</sup> Equipment**

A non-invasive home treatment solution

#### FLOWOX™





#### **Control Unit**

Multi patient use - multiple treatment cycles

#### Pressure Chamber (Boot):

Single patient use – multiple treatment cycles



#### Consumables

Strap, seal, padding are consumables that will need to be replaced after each treatment cycle – 180 hours.

#### **Technical Specs**

- Control Unit (CU)
- Packaged CU
- Dimension Packed CU
- Pressure Chamber (PCH)
- Packaged PCH
- Dimension Packed PCH

2,9 kg 4,5 kg (incl. power supply) 38 x 35 x 56 cm 2,1 kg 4,5 kg (incl. assembly parts) 57 x 31 x 48 cm

### FLOW**OX**™

Intermittent Negative Pressure Therapy





HOME TREATMENT

## How does the FlowOx<sup>™</sup> treatment work?

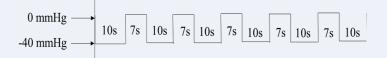
FlowOx<sup>™</sup> works by "exercising" the peripheral blood circulation.

#### FLOWOX™

#### How?

Through repeating shifts between a light negative pressure (-40 mm Hg) and normal atmospheric pressure, the natural dynamics and function of the vascular system is exercised. Everything from the arteries to the capillaries in the outer layers of the skin experience the fluctuations and thereby improving supply of oxygen and nutrients which is essential for maintaining and restoring the normal function of the skin and musculature.

FlowOx<sup>™</sup> thus addresses the underlying problems caused by poor peripheral circulation.



Intermittent negative pressure applied by FlowOx<sup>™</sup>

Seal

### **Clinical Data and Evidence**

FlowOx<sup>™</sup>, INP Therapy, Blood Flow

- ✓ Blood Flow
- ✓ Flow Mediated Dilation and Shear Stress
- ✓ Improved walking capacity



## The mechanisms of action of FlowOx<sup>™</sup> have been carefully studied through the years

FlowOx<sup>™</sup> is indicated for the treatment of PAD, e.g. with intermittent claudication or rest pain, and/or wounds. Other relevant indications include foot and lower leg ulcers of mixed aetiology associated with immobility such as paraplegia following spinal injury, and diabetic and non-diabetic arteriopathic foot and leg ulcers.

Early long-term testing documents increased blood flow, pain reduction, wound healing and amputation prevention.

#### Here is a selection of the most relevant studies.

- The acute effect of INP Therapy on Blood Flow Parameters
- The Scientific Journey of FlowOx™
- Blood flow parameters with INP Mechanism of action with FlowOx<sup>™</sup>
- Flow Mediated Dilation & Shear Stress Mechanism of action with FlowOx<sup>™</sup>
- Improved walking capacity: Publications of the impact on primary clinical endpoints







### **The Scientific Journey**

of  $FlowOx^{{\scriptscriptstyle {\rm TM}}}$ 

For a complete overview of all publications please refer to page 35.



#### **2016** STUDY

Application of **intermittent negative pressure on the lower extremity** and its effect on macro- and microcirculation in the foot of healthy volunteers.

Author: Sundby et. al. 2016.

### 1934

#### STUDY

The idea of "**Intermittent Negative Pressure**" was first conceived in the 1930's by Herman and Reid.

Hermann and Reid; Arch Surg. 1934;29(5):697-704

### 2010

Development of the FlowOx<sup>™</sup> Concept in Norway.

### 2017

#### STUDY

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т

The acute effects of lower limb intermittent negative pressure on foot macro- and microcirculation in patients with peripheral arterial disease.

Author: Sundby et. al. 2016.

### 2019

#### STUDY

The acute effects of lower limb intermittent negative pressure on foot macro-and microcirculation in patients with peripheral arterial disease.

Author: Hoel et. al. 2019.

### 2020

#### STUDY

Treament with intermittent negative pressure (INP) for intermittent claudication (Impact on primary clinical endpoints) A Randomized Controlled Trial (RCT)

Author: Hoel et. al. 2020.

### 2021

#### STUDY

Effects of intermittent negative pressure treatment on circulating vascular biomarkers in patients with intermittent claudication Biomarkers.

Author: Hoel et al. submitted 2021.

### 2019

#### STUDY

Fluctuation in shear rate, with unaltered mean shear rate, improves brachial artery flow-mediated dilation in healthy, young men.

Author: Holder et. al. 2019.

### 2021

#### STUDY

Follow-up trial: Walking distance after 24 weeks. Treatment with intermittent negative pressure (INP) for intermittent claudication (IC) (Impact on primary clinical endpoints) 12 week follow up trial.

Author: Hoel et al. submitted 2021.

### 2021

#### STUDY

**Economic model to examine the cost-effectiveness** of FlowOx home therapy compared to standard care in patients with

peripheral artery disease.

Author: Ezeofor et al., 2021.





### **Studies on the Acute Effect**

Of INP Therapy on Blood Flow Parameters

#### CLINICAL DATA AND EVIDENCE

Over the past few years, **INP Therapy** has gained significant attention for its potential to **improve cardiovascular health.** The following studies from 2016, 2017, and 2019 focus on the acute effect of INP therapy on blood flow parameters.

The effects of FlowOx<sup>™</sup> and INP are based on basic physical principles and have been **well-researched and documented in clinical studies.** 

These studies have been done on both **healthy individuals** and **PAD patients**. Both results have shown positive effects of FlowOx<sup>™</sup>.

Results from studies focused on determining the optimal pressure level that would achieve the desired result without causing unnecessary pain or stress to the patient. The FlowOx<sup>™</sup> treatment is suitable for patients who are struggling with ischemic wounds, painful walking, painful resting and painful, slow recovery from surgical revascularization.

#### Read the complete studies at <u>www.flowox.com</u>

#### **STUDY**

#### **STUDY CONCLUSION**

### 2016

Application of intermittent negative pressure on the lower extremity and its effect macroand microcirculation in the foot of healthy volunteers.

Author: Sundby et. al. 2016.

#### 2017

The acute effects of lower limb intermittent negative pressure on foot macro- and microcirculation in patients with peripheral arterial disease

Author: Sundby et. al. 2016.

#### 2019

The acute effects of different levels of intermittent negative pressure on peripheral circulation in **patients** with peripheral artery diesase.

Author: Hoel et. al. 2019.

#### 2019

#### Fluctuation in shear rate, with unaltered mean shear rate, improves brachial artery flow-mediated dilation in healthy, young men.

Author: Holder et. al. 2019.

**INP of -40 mmHg** in the foot in healthy volunteers induced rhythmical fluctuations in blood flow and increased both arterial blood flow velocity and skin blood flow.

This was the first study to describe the effects of INP on skin blood flow and arterial blood flow velocity. The first to compare different sequences of negative pressure oscillations on lower limb perfusion.

The study found that **INP increases foot macro- and microcirculatory flow pulsatility.** Application of INP resulted in increased mean arterial blood flow velocity.

The study found that **INP of -40 and -60 mmHg** applied in cycles of 10 sec of negative pressure and 7 sec of atmospheric pressure **induced acute increase in arterial and skin blood flow.** 

### The study found that INP induces fluctuations in blood flow and shear rate that improves endothelial function.

This may represent a hemodynamic stimulus improving vascular health.

The Holder et al study started to shed light on the longer term mechanism of action for **FlowOx™**.



### **Blood Flow Parameters with INP**

Mechanism of Action with FlowOx™

#### CLINICAL DATA AND EVIDENCE

When applying INP in combination with FlowOx™, the level of impact is visible in the skin blood flow and the fluctations in the arterial flow.

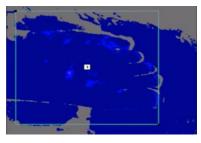
These blood flow parameters show the differences in the arteries and veins during the active phase as opposed to the passive phase.

### Increased fluctuations in skin blood flow

The pictures on the right show the laser speckle imaging of the skin during FlowOx™ treatment. The active phase photo shows a bright blue color which indicates the increased skin perfusion.

#### PASSIVE PHASE

#### ACTIVE PHASE



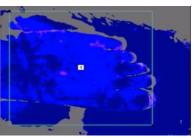


Photo: Laser speckle imaging of the skin during FlowOx™ treatment.

### Increased fluctuations in arterial flow

The picture of the active phase shows an increased amplitude from the baseline which indicates an increaced arterial blood flow.

#### PASSIVE PHASE



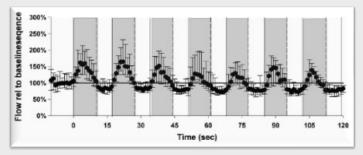
#### ACTIVE PHASE



Photo: Ultra sound Doppler measurement: Dorsalis pedis of a PAD patient.



## FlowOx<sup>™</sup> Therapy affects the baseline sequence



Sundby et. al. 2016

The black dotted lines illustrate the measurements of the blood flow when applying intermittent negative pressure.



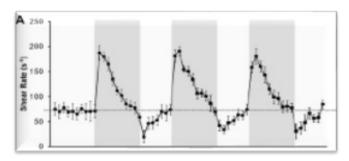
### **Flow Mediated Dilation & Shear Stress**

Mechanism of Action with  $FlowOx^{TM}$ 

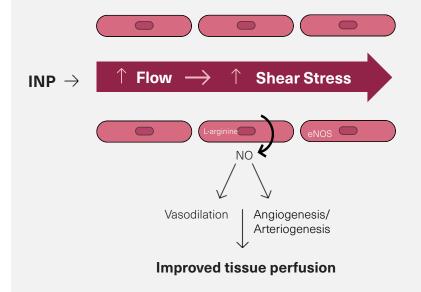
#### CLINICAL DATA AND EVIDENCE

Treatment with FlowOx<sup>™</sup> increases shear stress, which acts as a positive stimulus on the endothelium, resulting in improved tissue perfusion.

For patients with PAD, FlowOx<sup>™</sup> increases the capacity of the vasculature, including existing collaterals.



This figure shows the variations in blood flow when applying FlowOx.



#### **Shear Stress**

The vascular endothelium is exposed to a hemodynamic stress generated by the blood flow known as the wall shear stress. Wall shear stress is defined as the force per unit area exerted on the vessel wall by the blood flow and it depends on blood viscosity and the blood flow velocity profile.

**Vasodilation** is the dilation, or widening, of blood vessels.

**Angiogenesis** is the growth of new blood vessels.

**Arteriogenesis** is the remodeling of existing collaterals.

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### **Treament with intermittent negative pressure (INP) for intermittent claudication**

#### A Randomized Controlled Trial (RCT)

Henrik Hoel, MD, Erik Mulder Pettersen, MD, Lars Øivind Høiseth, MD, PhD, lacob Mathiesen, PhD, Arne Seternes, MD, PhD, and Jonny Hisdal, PhD.

#### CLINICAL DATA AND EVIDENCE

**The objective** of this study was to investigate the effects of lower extremity INPtreatment for 1 hour two times daily for 12 weeks on the walking distance of patients with intermittent claudication (IC).

#### **Enrollment and allocation**

In the enrollment of the claudicant RCT, 85 patients were assessed for eligibility.

#### PWD = Pain-Free Walking Distance MWD = Maximal Walking Distance

72 patients were randomized into 2 groups:

- 38 patients were allocated to -40 mmHg INP treatment
- 34 patients were allocated to -10 mmHg INP treatment.

All patients went through 12 weeks of treatment without knowing what type of group they were in.





### Results after 12 weeks: Improved walking distance

Treatment with INP for intermittent claudication

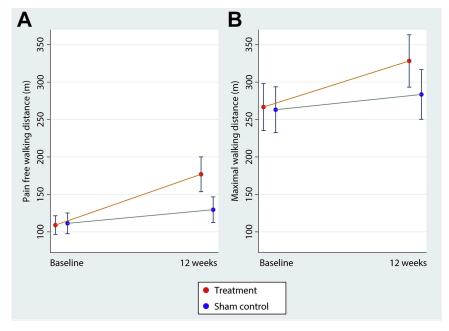
**The results of the study** demonstrate that treatment with -40 mm Hg INP for one hour in the morning and one hour in the evening for 12 weeks resulted in an increase in pain-free walking distance (PWD) compared to sham treatment in patients with IC.

#### Pain-Free Walking Distance (PWD)

The PWD for the active treatment group showed an increase of 68 meters after 12 weeks, while the sham treatment group showed an increase of 18 meters.

#### Maximal Walking Distance (MWD)

The MWD for the active treatment group showed an increase of 62 meters, while the sham treatment group showed an increase of 20 meters.



Hoel H et al. J Vasc Surg. 2021



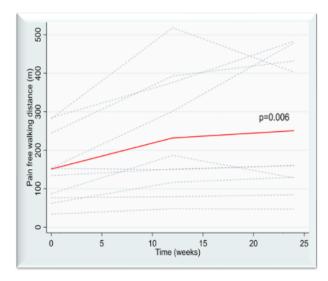


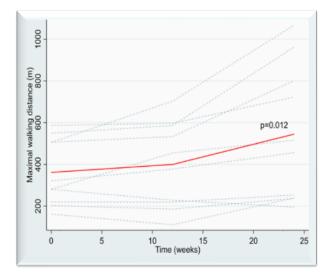
### Follow-up trial: Walking distance after 24 weeks

Treatment with intermittent negative pressure (INP) for intermittent claudication (IC)

#### **CLINICAL DATA AND EVIDENCE**

Hoel, Henrik; Pettersen, Erik Mulder; Høiseth, Lars Øivind; Mathiesen, Iacob; Seternes, Arne; Hisdal, Jonny





Hoel H et al. Ann Vasc Surg. 2021

The Claudicant RCT Follow-Up trial conducted by Hoel H. et. al. examined the walking distance after 24 weeks of treatment.

Ten patients who received the -40 mmHg INP treatment participated in the Follow-Up trial. These results provide valuable insights into the efficacy of the FlowOx<sup>™</sup> therapy for improving walking distance in patients with IC. **The results** showed a mean increase in the Pain-Free Walking Distance (PWD) of 100 meters after 24 weeks of treatment with the FlowOx<sup>™</sup> device (p=0.006).

Additionally, the Maximal Walking Distance (MWD) showed a mean increase of 183 meters after 24 weeks (p=0.012). 10 patients given the -40 mmHg INP treatment were enrolled in the Follow up trial.

RESULTS OF FOLLOW-UP TRIAL

100 Meter Increase

Pain-free Walking Distance

RESULTS OF FOLLOW-UP TRIAL

**183** Meter Increase Maximal Walking Distance





### **Impact on Secondary Clinical endpoints**

Wound Healing & Leg Ulcers

#### CLINICAL DATA AND EVIDENCE

Conducting research on wound healing and foot ulcers is a very complex and difficult process due to several factors:

- » Complexity of the condition
- » Variability in patient populations
- » Difficulty in measuring outcomes
- » Limited evidence base

Despite these challenges, there have been promising results from physiological case reports that have explored the use of FlowOx<sup>™</sup> treatment for wound healing and foot ulcers. These studies offer a glimpse into the potential benefits of this treatment and suggest the need for further research in this area.





### **Impact on Secondary Clinical endpoints**

Reports on using INP therapy on wounds & leg ulcers

#### **Case Report**

PHYSIOLOGICAL REPORTS

The effects of intermittent negative pressure on the lower extremities' peripheral circulation and wound healing in four patients with lower limb ischemia and hard-to-heal leg ulcers: a case report

Øyving H. Sundby<sup>1,2,3</sup>, Lars Ø. Høiseth<sup>1,4</sup>, lacob Mathiesen<sup>3</sup>, Jørgen J, Jørgensen<sup>2,5</sup> & Jonny Hisdal<sup>1</sup>

#### RESULT

"In these cases, involving patients with hard-to-heal leg and foot ulcers, observed that **INP therapy improved** ulcer healing considerably."

> "Foot perfusion improved after completion of 8 weeks of INP-therapy."

#### **Case Report**

PHYSIOLOGICAL REPORTS

Intermittent mild negative pressure applied to the lower limb in patients with spinal cord injury and chronic lower limb ulcers: a crossover pilot study

Øyving Heiberg Sunby<sup>1,2,3</sup>, Ingebjørg Irgens<sup>2,4</sup>, Lars Ø. Høiseth<sup>1,5</sup>, Iacob Mathiesen<sup>3</sup>, Eivind Lundgaard<sup>4</sup>, Hanne Haugland<sup>6</sup>, Harald Weedon-Fekjær<sup>7</sup>, Jon O. Sunhagen<sup>8</sup>, Gunnar Sandbæk<sup>2,9</sup>, Jonny Hisdal<sup>1</sup>.

#### RESULT

"INP therapy can be used as a home-based treatment for patients with SCI and chronic lower U limb ulcers."





### **Published Papers**

On FlowOx<sup>™</sup> and INP

- 1. Application of intermittent negative pressure on the lower extremity and its effect on macro- and microcirculation in the foot of healthy volunteers, *Sundby et al; Physiol Rep, 4 (17), 2016*
- 2. The acute effects of different levels of intermittent negative pressure on peripheral circulation in patients with peripheral artery disease; *Hoel et al.; Physiol Rep,* 7 (20), 2019
- 3. The acute effects of lower limb intermittent negative pressure on foot macro- and microcirculation in patients with peripheral arterial disease; *Sundby et al.; PLoS ONE 12(6): e0179001.*
- 4. Intermittent negative pressure applied to the lower limb increases foot macrocirculatory and microcirculatory blood flow pulsatility in people with spinal cord injury; Sundby et al.; Spinal Cord https://doi.org/10.1038/s41393-017-0049-8
- 5. Fluctuation in shear rate, with unaltered mean shear rate, improves brachial artery flow-mediated dilation in healthy, young men; *Holder et al.; J Appl Physiol 126:* 1687–1693, 2019
- 6. A randomized controlled trial of treatment with intermittent negative pressure for intermittent claudication, Hoel et al.; Journal of Vascular Surgery, vol. 73, no. 5
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