COMPRESSION, OXYGEN AND HUMIDIFICATION

Reduced Inflammation
Improved Wound Healing
Decreased Wound Recurrence

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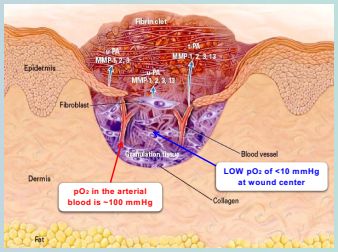
INTRODUCTION: Key Elements of Wound Healing

- Tissue oxygenation (perfusion)
- Effective resolution of inflammation

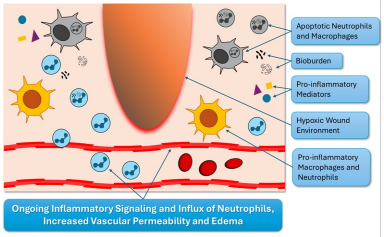


CHRONIC WOUNDS ARE HYPOXIC

Chronic wounds are inherently hypoxic due to inflammatory factors, microvascular disruption and elevated metabolic demand

Adequate tissue oxygenation is necessary for:

- Immune response (NADPH/oxidative burst)
- Resolution of inflammation
- Angiogenesis
- Collagen synthesis and crosslinking

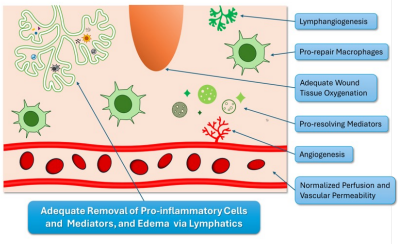


EFFECTS OF EDEMA ON WOUND HEALING

- Decreased tissue perfusion
- Inadequate removal of inflammatory mediators by lymphatics
- Amplified recruitment and activation of immune cells
- Increased metabolic demand
- Hypoxic wound environment
- Increased risk of infection
- Delayed healing

ROLE OF THE LYMPHATICS IN THE RESOLUTION OF INFLAMMATION

Removal of inflammatory mediators and excess interstitial fluid from the wound environment is necessary to reduce inflammatory signaling, restore tissue perfusion and initiate the proliferative phase of healing. **This is done predominantly through activation of the lymphatics.**



OBJECTIVE

- Investigate the effects of **cyclical limb compression** and **pressurized topical oxygen – multi-modality topical oxygen therapy (MMTOT)**, for the treatment of chronic lower extremity wounds in a real-world setting

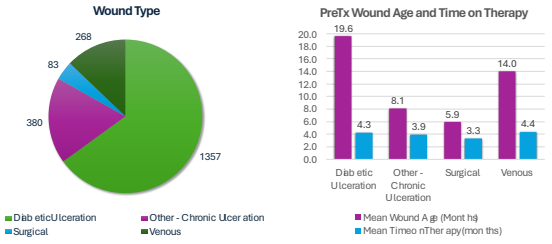
METHODS

- Outcomes data were collected for patients treated with concurrent **cyclical limb compression** and **pressurized topical oxygen (MMTOT)** for **distal lower extremity wounds** between January 2023 and September 2024
- There were no exclusion criteria other than lack of available data and withdrawal from treatment

RESULTS

- 2911 patients were treated with MMTOT therapy for distal lower extremity wounds between January 2023 and September 2024
- 700 did not complete therapy due to non-medical patient-related factors, or a change in treatment plan
- Outcomes of the remaining 2088 patients were analyzed

ALL WOUNDS (n=2088)



DIABETIC FOOT ULCER/SURGICAL

ARTERIAL/VENOUS/SURGICAL

SURGICAL/VENOUS

VENOUS LEG ULCER – present >5 years

Start of Therapy | Week 12 | Week 24

Lower Extremity Wounds Treated with Intermittent Compression and Pressurized Topical Oxygen Jan. 2023 – Sept. 2024

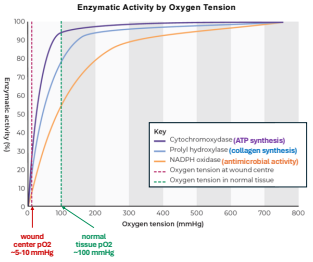
	Healed	Sufficient Wound Improvement	Medical Hold	Hospitalized	Hospice/ Palliative care	Amputation	Deceased (Not Product Related)	Grand Total
Diabetic Ulceration								
Therapy Outcome: n	1032	6	18	68	13	120	100	1357
Therapy Outcome: %	76.1%	0.4%	1.3%	5.0%	1.0%	8.8%	7.4%	100.0%
Mean Wound Age: months (SD)	10.8 (11.4)		5.0*	211.2 (447.1)	9.0*	14.1 (22.8)	10.9 (15.5)	19.6 (93.1)
Mean Time on Therapy: months (SD)	4.4 (2.8)	5.5 (6.3)	4.0 (3.9)	4.0 (3.3)	2.4 (1.7)	3.6 (2.2)	4.2 (3.0)	4.3 (2.8)
Wound Recurrence: n (%)	40 (2.5%)							
Multimorbid Chronic LE Ulceration								
Therapy Outcome: n	303		9	20		20	28	380
Therapy Outcome: %	79.7%		2.4%	5.3%		5.3%	7.4%	100.0%
Mean Wound Age: months (SD)	7.9 (11.7)		9.0*	11.5 (11.9)		6.3 (1.5)	8.1 (6.7)	8.1 (11.1)
Mean Time on Therapy: months (SD)	3.9 (2.8)		4.6 (3.0)	3.6 (2.4)		3.6 (2.4)	4.3 (3.9)	3.9 (2.9)
Wound Recurrence: n (%)	2 (0.1%)							
Surgical								
Therapy Outcome: n	64	1		5	1	7	5	83
Therapy Outcome: %	77.1%	1.2%		6.0%	1.2%	8.4%	6.0%	100.0%
Mean Wound Age: months (SD)	5.8 (5.6)	7.0*		8.0 (7.2)		4.0*	3.0*	5.9 (5.4)
Mean Time on Therapy: months (SD)	3.3 (2.2)	2.5		3.6 (3.1)	0.9*	2.9 (1.8)	4.2 (2.5)	3.3 (2.2)
Wound Recurrence: n (%)	0 (0.0%)							
Venous								
Therapy Outcome: n	193	1	12	21	1	13	27	268
Therapy Outcome: %	72.0%	0.4%	4.5%	7.8%	0.4%	4.9%	10.1%	100.0%
Mean Wound Age: months (SD)	11.2 (9.6)		8.0*	23.6 (32.6)			20.5 (21.9)	14.0 (16.8)
Mean Time on Therapy: months (SD)	4.6 (2.9)	2.3*	3.2 (2.1)	3.6 (2.1)	2.3*	2.7*	5.3 (3.9)	4.4 (2.9)
Wound Recurrence: n (%)	8 (0.5%)							
Therapy Outcome: n	**1592**	**8**	**39**	**114**	**15**	**160**	**160**	**2088**
Therapy Outcome: %	**76.2%**	**0.4%**	**1.9%**	**5.5%**	**0.7%**	**7.7%**	**7.7%**	**100.0%**
Mean Wound Age: months (SD)	**9.4 (11.4)**	**7.0**	**7.3 (2.1)**	**55.4 (200.2)**	**9.0**	**11.3 (15.7)**	**11.0 (14.0)**	**13.5 (51.0)**
Mean Time on Therapy: months (SD)	**4.3 (2.8)**	**4.7 (5.6)**	**3.9 (3.2)**	**3.8 (2.9)**	**2.3 (1.6)**	**3.5 (2.2)**	**4.4 (3.3)**	**4.2 (2.9)**
Healed Wound Recurrence: n (%)	**50 (3.1%)**							

*SD: standard deviation; *insufficient data for SD*

Discussion

EFFECTS OF INCREASING TISSUE OXYGEN

- Upregulated leukocyte and NADPH Oxidase function results in **increased reactive oxygen species (ROS) production and pathogen killing**
- Increased expression of angiogenic growth factors (VEGF, PDGF) results in **greater density and quality of neovascularization**
- Upregulation of prolyl hydroxylase allows fibroblast cells (via lysine and proline pathway) to lay down **better-quality triple helix collagen fibrils with greater tensile strength**

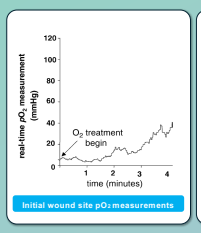


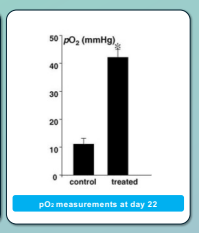
Adapted From: Journal Of Wound Care Consensus Document Vol 32, No 8 (Suppl 8b), August 2023

THE EFFECTS OF OXYGEN ON TISSUE QUALITY

- **Collagen deposition provides the matrix for angiogenesis and tissue remodeling**
- **The enzymes responsible for the triple helix configuration and crosslinking of collagen are directly oxygen dependent**
- **Collagen crosslinking is responsible for healed tissue tensile strength**
- **Optimal collagen deposition occurs at tissue pO_2 of 250 mmHg (well above normal tissue pO_2)**
- **Oxygen supplementation results in superior collagen deposition and tissue strength**

Dermal Excisional Wound Healing In Pigs Following Treatment With Topically Applied Pure Oxygen



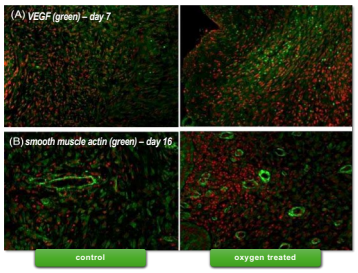


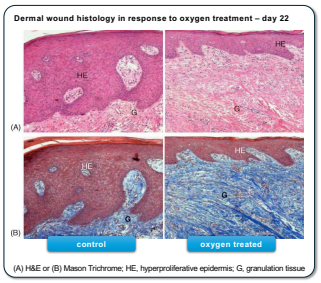
Fries et al. - Mutation Research, August 2005

- Exposure of open dermal wounds to topical oxygen treatment increased tissue pO2 of superficial wound tissue
- Tissue pO_2 increased within the first 4 minutes of exposure
- Repeated treatment accelerated wound closure
- Elevated pO_2 was sustained at day 22

Dermal Excisional Wound Healing In Pigs Following Treatment With Topically Applied Pure Oxygen

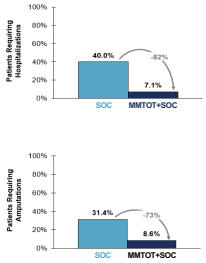
- O2 treatment induces VEGF mRNA levels in endothelial cells and macrophages and increases VEGF protein expression
- Oxygen treated wounds show signs of improved angiogenesis





Dermal Excisional Wound Healing In Pigs Following Treatment With Topically Applied Pure Oxygen

- Advanced remodeling and healing in the treated as compared to the control group
- Well demarcated dermal epidermal junction
- Well developed peg layer
- Organized basal cell layer
  - Less scaring – improved tensile strength
  - Healthy desquamation reduced callus formation



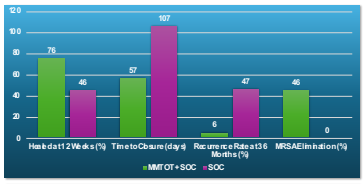
Reduced Hospitalizations and Amputations in Patients with Diabetic Foot Ulcers Treated with Cyclical Pressurized Topical Wound Oxygen Therapy: Real-World Outcomes

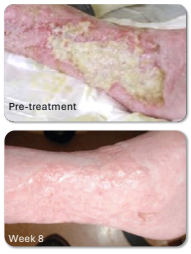
Yellin, et al. – Advances in Wound Care, November 2022

- 200+ comorbid veterans with DFU
- **82% reduction in hospitalizations** (p<0.0001)
- **73% reduction in amputations** (p=0.0007)
- **9x lower risk of wound-related hospitalization** (OR: 8.667; 95% CI: 3.101, 24.219; p < 0.0001)
- **5x lower risk of amputation** (OR: 4.887; 95% CI: 1.840–12.985; p = 0.0015)

Technical and Clinical Outcome of Topical Wound Oxygen in Comparison to Conventional Compression Dressings in the Management of Refractory Nonhealing Venous Ulcers

Tawfick et al. Vascular and Endovascular Surgery, 2012





CONCLUSIONS

- Hypoxia, inflammation and dysregulated lymphatic function (edema) are characteristic of most lower extremity chronic wounds
- **By addressing both edema and tissue hypoxia, this combination therapy reduces inflammation and pain, increases tissue perfusion, improves healing, and decreases wound recurrence**