

Topical Oxygen Therapy for Wound Bed Optimization Prior to Planned Skin Substitute Application: A Four-Patient Case Series

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INTRODUCTION

Chronic lower-extremity wounds remain challenging to manage, particularly in patients with diabetes, neuropathy, vascular disease, venous insufficiency, or those recovering from complex foot and ankle surgery. Persistent inflammation, impaired angiogenesis, poor perfusion, and tissue hypoxia contribute to stalled granulation and delayed healing.^{1–3} Oxygen plays a central role in fibroblast activity, collagen synthesis, angiogenesis, epithelialization, and immune defense; while transient hypoxia supports normal healing physiology, sustained hypoxia disrupts tissue regeneration.^{2,3} Topical Oxygen Therapy (TOT) delivers supplemental oxygen directly to the wound surface and has demonstrated improved healing outcomes in diabetic foot ulcers when added to standard care, as supported by meta-analyses and randomized trials.^{1,4–6} However, beyond facilitating closure, Continuous Topical Oxygen Therapy (cTOT) may support wound-bed optimization in complex wounds preparing for grafts or skin substitutes. Achieving a well vascularized, granulating wound bed is essential for successful tissue incorporation and advanced closure. This case series evaluates cTOT as a bridge therapy for stalled or complex lower-extremity wounds requiring wound-bed preparation prior to grafting. Four patients received cTOT alongside standard wound care, with near infrared (NIR) hemoglobin oxygenation imaging used to assess local tissue oxygenation and microvascular perfusion throughout treatment.

CONTINUOUS TOPICAL OXYGEN THERAPY (cTOT)

The cTOT device delivers a low flow of continuous supplemental oxygen directly to the wound through an oxygen delivery system. By increasing local oxygen availability, cTOT is designed to support key processes involved in wound healing, including cellular proliferation, collagen synthesis, angiogenesis, epithelialization, and host immune function. In this case series, cTOT was used as an adjunct to standard wound care to promote wound-bed optimization and healthy granulation prior to advanced tissue coverage.

REFERENCES

1. The efficacy of topical oxygen therapy for wound healing: A meta-analysis of randomized controlled trials and observational studies. Seven RCTs (n=692) and two controlled observational studies (n=111) were included; adjunctive TOT was associated with a higher proportion of healed wounds.
2. Sykorová A, et al. Topical oxygen therapy and singlet oxygen in wound healing: A scoping review. *Int Wound J*. 2024. The review included 49 studies and discusses the roles of oxygen in fibroblast/keratinocyte proliferation, collagen synthesis, angiogenesis, and immune function.
3. Sen CK, et al. Evidence-Based Recommendations for the Use of Topical Oxygen Therapy in the Treatment of Lower Extremity Wounds. Provides mechanistic discussion of wound hypoxia, oxygenation, angiogenesis, collagen deposition, and tissue repair.
4. Carter MJ, Frykberg RG, Oropallo A, Sen CK, Armstrong DG, Nair HKR, Serena TE. Efficacy of Topical Wound Oxygen Therapy in Healing Chronic Diabetic Foot Ulcers: Systematic Review and Meta-Analysis. *Adv Wound Care*. 2023;12(4):177–186. doi:10.1089/wound.2022.0041. Four RCTs were included; pooled complete-healing RR was 1.59 (95% CI 1.07–2.37).
5. Systematic review of the effects of topical oxygen therapy on wound healing. *JVS–Vascular Insights*. 2024;2:100051. Twenty-two studies were reviewed; the authors found evidence of benefit while emphasizing substantial heterogeneity and risk of bias in the literature.
6. Topical oxygen therapy in the treatment of diabetic foot ulcers: a multicentre, open, randomised controlled clinical trial. In 145 randomized patients, 44.4% receiving topical oxygen plus standard care achieved closure at 12 weeks compared with 28.1% receiving standard care alone; mean wound-area reduction was also greater with adjunctive TOT.

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CASES

Case 1: 53M. Chronic diabetic/Charcot wound present >1 year despite total contact casting (TCC), offloading, Medihoney, hyperbaric oxygen therapy (HBOT), and multiple surgical debridements. Positive probe-to-bone, but MRI was negative for osteomyelitis (OM).

Baseline	6 weeks	18 weeks
4.5 x 4 cm Grade 4	1 x 1.4 cm	0.2 cm ²
 NIRS Imaging: Regional tissue oxygenation of 34–50%		

Case 2: 56M. Diabetic with history of lymphedema, neuropathy, hypertension (HTN), and peripheral artery disease (PAD) presented with a full-thickness plantar ulcer extending to fascia with keratotic borders. Wound present >1 year despite TCC, HBOT, and multiple debridements and local care with various modalities. No clinical signs of infection.

Baseline	1 week	8 weeks
1.7 cm ² Grade 3		Fully epithelialized wound and closed, obviating the need for the planned graft
	 NIRS Imaging: Regional tissue oxygenation of 62% and 58%	

Case 3: 66M. Diabetic with Charcot neuroarthropathy and a history of HTN, hyperlipidemia, and chronic OM presenting with a chronic full-thickness rearfoot ulcer with heavy serous drainage and a sinus tract probing to bone. Wound present >1 year despite conservative treatment including TCC and multiple local modalities. OM was treated with oral antibiotics until cured.

Baseline	6 weeks	11 weeks	15 weeks
4.1 x 4.2 x 0.4 cm Grade 4		Robust granulation tissue with progressive wound contraction and decreased wound depth	Complete epithelialization with full wound closure
 NIRS Imaging: Regional tissue oxygenation of 59–89%	 NIRS Imaging: Regional tissue oxygenation of 94–98%		

Case 4: 54M. History of thromboembolic disease (DVT), transmetatarsal amputation (TMA), and multiple renal and cardiovascular comorbidities, rendering him a high-risk surgical candidate. Presented with a full thickness wound with macerated borders, fibrinous heavy serous drainage, and a duration of 1 year, despite TCC, HBOT, offloading, and multiple debridements. No OM.

Baseline	19 weeks	32 weeks	37 weeks
5.5 cm ² Grade 3	3.8 cm ²	3.2 cm ²	2.7 cm ² 49.1% reduction

METHODS

An ongoing retrospective case series included four adults (53–66 years) with complex diabetic, ischemic, venous, or postoperative foot and ankle wounds. Wounds ranged from stalled fibrogranular beds to full thickness defects with exposed muscle or bone (2.2 × 1.6 × 0.2 to 7.0 × 4.0 × 0.2 cm). All wounds underwent sharp excisional debridement to viable bleeding tissue as clinically indicated. Continuous Topical Oxygen Therapy (cTOT) was incorporated into individualized standard wound care to optimize wound bed quality prior to planned graft or skin substitute application. Standard care included local wound care, offloading, edema control, antimicrobial dressings when indicated, and management of medical and vascular comorbidities. Serial examinations assessed wound dimensions, depth, tissue quality, granulation, devitalized tissue, wound edge stability, coverage of exposed structures, and overall graft readiness. Near infrared spectroscopy (NIRS) hemoglobin oxygenation imaging was used adjunctively to evaluate local tissue oxygenation and microvascular perfusion during wound bed preparation.

RESULTS

All four patients demonstrated favorable clinical progression following incorporation of continuous topical oxygen therapy (cTOT). Across the series, wounds showed increased healthy granulation tissue, reduced devitalized tissue, improved wound edge stability, and overall wound bed optimization despite varied etiologies and comorbidities. **Two of four patients (50%) achieved complete wound closure during continued wound bed preparation, eliminating the need for their originally planned graft or skin substitute.** The remaining two patients demonstrated ongoing improvement in granulation tissue and wound bed quality and remain actively healing. Individual wound responses included progressive granulation and coverage in a postoperative wound dehiscence; improved depth, granulation, and stability in diabetic and venous ulcers; rapid granulation and wound contraction in a full thickness ulcer following bone excision; and stable granulation with progressive coverage of exposed muscle and bone in complex bilateral wounds. Near infrared (NIR) hemoglobin oxygenation imaging provided adjunctive physiologic assessment of local tissue oxygenation and microvascular perfusion throughout treatment. Overall, 4/4 patients (100%) demonstrated improved wound bed characteristics, and 2/4 (50%) achieved complete closure without the planned advanced tissue coverage.

CONCLUSION

This four-patient case series suggests that continuous topical oxygen therapy (cTOT) may support wound bed optimization in complex lower extremity wounds preparing for graft or skin substitute application. Despite substantial healing barriers—including diabetes, vascular compromise, venous disease, postoperative dehiscence, complex foot deformities (charcot) and exposed deep structures—all patients demonstrated progressive improvement in granulation tissue, wound edge stability, and overall wound bed viability following incorporation of cTOT into comprehensive wound care. cTOT functioned as a potential bridge therapy, converting compromised or poorly granulated wounds into healthier recipient beds suitable for advanced closure. Two patients ultimately healed to full closure during wound bed preparation, eliminating the need for their originally planned graft or skin substitute, while the remaining patients continued to show meaningful improvement in granulation and coverage of exposed structures. Near infrared spectroscopy(NIRS) hemoglobin oxygenation imaging provided complementary physiologic insight into local tissue oxygenation and microvascular perfusion, aligning with observed clinical improvements in wound bed quality. These findings support further investigation of cTOT as a tool for enhancing wound bed readiness and facilitating advanced closure.