

Multicenter DFU Study: Results from a **Tier 1A (prospective, fully-blinded with placebo) Diabetic Foot Ulcer** clinical trial involving **146 patients** across 34 sites show that Continuous Diffusion of Oxygen (CDO) therapy to be **statistically significant** compared to a placebo arm. The study was **published in the Journal of Wound Care** in September of 2018¹. The rigor of this study is rare in the medical device world: it is a double-blind, prospective, randomly-controlled trial with a placebo and an active arm. Both arms received identical treatment (device, dressings, etc.) and the devices were functional in both arms. However, the oxygen did not flow to the wound in the placebo arm. In essence, this is on par with a pharmaceutical trial where the patients and clinicians do not know the treatment arm (removing patient and clinician bias). In simplest terms, the study evaluated standard of care Moist Wound Therapy (MWT) alone versus MWT plus continuous oxygen.

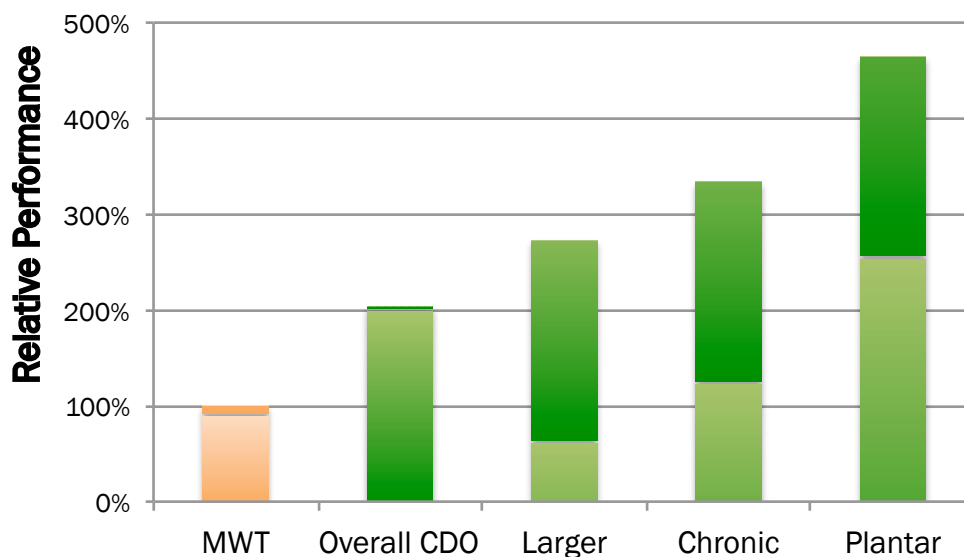
This study was designed and monitored in consultation with Centers for Medicare and Medicaid (CMS). CMS was concerned with effects of wound size and degree of wound chronicity (run-in period) and the study was designed to include both. **CMS cited the study design as the "Gold Standard" for how studies should be designed.** See reverse side for more details concerning the run-in period, placebo & study design.

Summary of Most Significant Results by Adding Oxygen Continuously:

- CDO closed significantly more wounds in 12 weeks: more than twice as many (204% that of MWT)
- CDO had a significantly faster time to 50% closure, almost half the time without oxygen
- CDO performs better:
 - as wounds get larger (273%, or 2.7x)
 - in more chronic wounds (334%, or 3.3x)
 - in wounds on the plantar aspect (465%, or 4.7x) which are potentially weight bearing
 - in populations more genetically predisposed to diabetes (257%, or 2.6x)
- CDO reduced the incidence of severe infections (75% fewer infections, no gangrene)

Summary from Abstract: A significantly higher proportion of people, more than twice as many (204%), healed in the active CDO arm compared to placebo (46% vs 22%, $P = .016$). This relative effect became greater in more chronic wounds: in the most chronic wounds, more than three times (334%) as many wounds closed in the active CDO arm (43.9% vs 13.2%, $P = .008$). Patients randomized to the active device experienced significantly faster rates of closure relative to the placebo ($P < .001$). As the wound size increased, the relative positive effect of CDO remained similar or became greater. **Dr. David Armstrong**, overall study principal investigator, summarized the results as **"The more you need CDO therapy, the better it appears to work"**.

Performance of CDO Relative to MWT



Study Setup (Unique Criteria which most other Published Studies Don't Have)

- Included a run-in period of two weeks, which primarily excluded:
 - Non-chronic wounds (wounds that were closing under standard of care)
 - Small wounds (wounds which typically show less difference with advanced therapy)
- NOTE:** the run-in period brought patients into the study and evaluated them for how fast the wound closed with MWT alone for two weeks under good standard of care (no device applied) – those that closed too quickly or became too small were excluded from the study
- Did not allow for other therapies to close wounds: some other studies, including VAC by Blume et al (see table at bottom), allow for amputation and surgical closure
- Analyzed for effect of wound size and chronicity on relative and absolute effectiveness
- Study Arms are identical with the exception that the Placebo MWT Arm had no oxygen flowing to the wound - eliminated bias of clinician and patient (see picture below)

Identical:

- Dressings
- Offloading
- Appearance
- Criteria
- Etc.



Comparison to other Published Studies (emphasize points above that other studies don't have)

- Outcomes with CDO are comparable to or better than other advanced wound healing treatments
- CDO is easier to use, patients can change own dressings (NPWT requires a clinician)
- This study uses only CDO or MWT to take wounds to full closure (other studies include closure using other interventions such as amputation & surgical closure in their results)
- Only this study is fully blinded – patients and clinicians in other studies can be biased

Study	Test Device (therapy)	Level of Evidence	Comparison Group	# of Subjects	Study Length, weeks	Wound Closure, Study Group**	Wound Closure, Control Group**	P-value	Relative Performance
Niederauer et al 2018	TransCu O ₂ (CDO)	1A	Placebo device MWT with specific foam and thin film, optional alginate	105	12	46%	22%	0.016	204%
Blume et al 2007	VAC (NPWT)	1B	MWT with alginates, foams, hydrocolloids, or hydrogels	335	16	43%	29%	0.007	148%
Marston et al 2003	Derma-graft (Skin Subs)	1B	Saline-moistened gauze	245	12	30%	18%	0.03	167%
Edmonds 2009	Apligraf (Skin Subs)	1B	Non-adherent dressing	72	12	52%	26%	0.03	200%

Reference:

1. Niederauer MQ, Michalek JE, Liu Q, Papas, Lavery LA, Armstrong DG. Continuous diffusion of oxygen improves diabetic foot ulcer healing when compared with a placebo control: a randomised, double-blind, multicentre study. J Wound Care 27(9):s30-s45 2018.