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# Continuous Diffusion of Oxygen Adjunct Therapy to Improve Scar Reduction after Cervicotomy – A Proof of Concept Randomized Controlled Trial ☆

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ABSTRACT

*Background:* Dressing materials are known to influence post-operative surgical wound healing and scar formation (SF). A particular dressing that could promote wound hydration is essential to ensure quick epithelialization and reduce SF. This study examined the effectiveness of a novel Continuous Diffusion of Oxygen (CDO) dressing to reduce scar length post cervicotomy.

*Methods:* A randomized controlled trial was performed in patients undergoing cervicotomy, either for thyroid or parathyroid disease. Patients were randomized to either control (CG) or intervention (IG) groups. The IG received a portable CDO system (TransCu O2, EO2 Concepts Inc., TX, USA), whereas the CG received a standard dressing for a 4-week period. The primary outcome was >10% of scar length reduction and %change in scar length.

*Results:* 21 patients were recruited (Age: 53 ± 16 years; 90% female; CG = 9, IG = 12). 5 patients were lost to follow-up. At 4 weeks, 88.8% of the IG significantly achieved >10% of scar reduction (versus CG = 28.5%, d = 0.48, $P = 0.049$), showing a 40.4% smaller scar (15.7% versus 11.2%, d = 0.13, $P = 0.72$) compared to the CG. However, the difference was not significant. A sub-sample of patients undergoing thyroidectomy showed a significant scar reduction using CDO (IG = 11.6% versus CG = 5.1%, d = 2.96, $P = 0.009$).

*Conclusions:* This is the first study to assess scar reduction using CDO adjunct therapy after cervicotomy. Advanced CDO dressings may assist wound healing showing improved out-

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comes for scar visualization in patients undergoing thyroidectomy. A larger sample is required to validate this observation.



## Introduction

Scar formation (SF) after surgical procedures may lead to physio and psychological concerns in some patients.[1] Such concerns may cause self-consciousness in individuals undergoing cervicotomy (e.g., anterior neck surgery) for either thyroid or parathyroid disease.[2] Recent studies on reducing scar post-cervicotomy have utilized different techniques for surgical closure such as the use of synthetic glue, subcuticular and intradermal absorbable sutures, or adhesive strips.[3, 4] However, a modest to no significant effect on reducing SF were reported; thus, aesthetic outcomes are still suboptimal and an alternative option might be able to address this gap.

Dressing materials are known to influence post-operative surgical wound healing and SF.[5-8] A particular dressing that could promote wound hydration is key to ensure quick epithelialization and decrease excessive SF. Technology has evolved into the development of systems able to extract oxygen from the atmosphere and transport it to tissues.[9] Applied oxygen to wounds has proven to stimulate collagen synthesis, matrix deposition, keratinocyte differentiation, and fibroblast migration, through cytokines and growth factors activated by the release of reactive oxygen species (ROS), which also play an antibacterial role in the wound site.[9-11] Moreover, oxygen may promote angiogenesis, and the process itself could be more efficient if the cutaneous tissue is sufficiently maintained oxygenated.[9, 12] Therefore, the level of transcutaneous oxygen could be a determinant factor of excessive SF[13].

Recently, different modalities for the application of oxygen to wounds have emerged.[14] Topical oxygen delivery therapy (TODT) has shown to vastly enhance wound healing through the previously mentioned factors, however with particular characteristics of not depending on local microvasculature[15] as well as the ability to be locally administered for long periods (e.g., until complete healing) representing no risk of systemic toxicity.[14] In addition, TODT facilitates deep osmotic hydration within the injured skin through the combination of vitamins, botanicals, antioxidants, and aminopeptides[16] which create an exponential increase in epidermal oxygen saturation.[17]

When administered continuously, TODT does not utilize pressure or require a chamber to function.[18] Current innovative TODT dressings have been proposed that support continuous diffusion of oxygen (CDO) to the wound bed, which in turn could promote faster wound hydration and quick epithelialization.[19] Nonetheless, most evidence for the effectiveness of CDO corresponds to lower extremity,[5-7, 20] pelvic,[21] or abdominal surgery[22, 23] wounds, and its application to reduce SF after cervicotomy has not been widely studied. The purpose of this study is to examine the effectiveness of a novel dressing with an add-on component of CDO to reduce scar length post-cervicotomy.

## Methods

### *Participants*

A randomized controlled trial (RCT) was performed in patients undergoing cervicotomy, either for thyroid or parathyroid disease. This study was approved by the local Institutional Review Board (IRB). All participants read and signed the IRB approved forms of informed consent before initiation of any assessment or data collection. The protocol of the study was registered in Clinicaltrials.gov-Identifier: NCT03960463. Inclusion criteria were age between 18 and 85 years old; presence of anterior neck surgical incision due to total or partial thyroidectomy due to hyperthyroidism, regardless of major cause (e.g., Graves disease, toxic nodular goiter, etc.) or parathyroidectomy due to hyperparathyroidism regardless of etiology (e.g., primary, secondary, tertiary); and willing to maintain a CDO system over the surgical incision site for a 4-week post-operative period. Participants meeting any of the following criteria were excluded: active drug/alcohol abuse; dementia or impaired cognitive function; excessive lymphedema; unable to comply with research appointments (e.g., long-travel); and history of or any undercurrent illnesses or conditions that could compromise the safety of the subject according to judgement of a qualified wound specialist.

### *Clinical measurements*

The demographic and comorbidity information included age, gender, body mass index (BMI), hyperthyroidism, hyperparathyroidism, diabetes mellitus (DM), chronic kidney disease (CKD), hypertension (HTN), dyslipidemia, depression, glucose count (mg/dL), wound length (cm), tissue oxygen saturation (SatO2), and the daily number of prescribed medications. All participants underwent clinical assessments such as Trauma Self Frailty Index,[24] the Global Patient-Reported Outcomes Measurement Information System (PROMIS-Global10),[25] Montreal Cognitive Assessment (MoCA),[26] Pittsburgh Sleep Quality Index (PSQI),[27] and Visual Analog Scale (VAS) for pain.[28]

### *Study design, CDO characteristics, and timeline*

One endocrine surgeon performed all the cervicotomies at a single institution. All wounds were closed in the same fashion. For the platysma layer, a 3–0 Vicryl suture SH needle with three

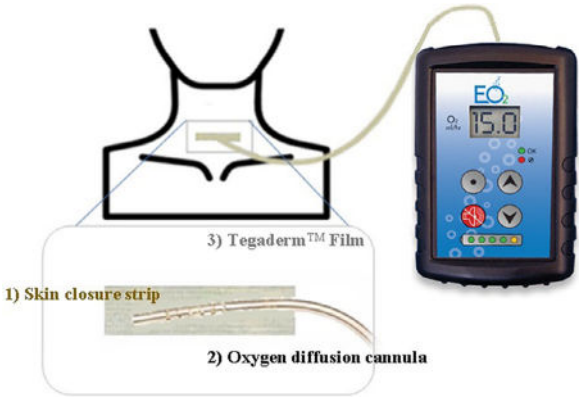


**Fig. 1 – CDO device and dressing adaptation to the anterior neck area. After closing the surgical site, a skin closure is placed followed by an Oxygen diffusion cannula (OxySpur, EO2 Concepts Inc., SA, TX, USA) protected by a Tegaderm Film (3M Healthcare, MN, US).**

interrupted stitches was used. For the skin layer, a 4–0 Stratafix on PS-2 needle subcuticular suture was used. No matisol, nor skin glue was utilized after wound closure.

Fig. 1 illustrates the CDO therapy placement. Patients were randomized ($n = 1{:}1$) to either control (CG) or intervention (IG) groups through a computer-generated list followed by sequential allocation concealment using sealed envelopes. The surgeon was not blinded to the group allocation. To deliver CDO, the IG received an FDA-Approved portable oxygen delivery system (TransCu O2®, EO2 Concepts Inc., SA, TX, USA)[6, 11] in the post-operative recovery area, immediately after leaving the operating room (OR). The system was placed by a trained research assistant as the following description. After surgical closure, a (0.5 × 4 in) reinforced skin closure strip (McKesson Medical-Surgical Inc., VA, US) was placed over the neck incision site for complete covering, followed by a (1 in) oxygen diffusion cannula (OxySpur®, EO2 Concepts Inc., SA, TX, USA) protected by a (2.3 × 2.7 in) Tegaderm™ Film (3M Healthcare, MN, US); all material was sterilized before utilization. The cannula was connected to an (72 in) oxygen delivery extension set (TransCu O2®, EO2 Concepts Inc., SA, TX, USA) that further was introduced to the portable device, which participants kept during the study period. Humidified oxygen was delivered at 5 ml/hr[18] in a pure continuous flow for 24 hours per day during a 4-week period. Following surgical closure, the CG received standard of care (SOC) using reinforced skin closure strips for the same period. All participants were monitored and clinically assessed on a weekly basis during the study duration. Each visit, the incision site was sterilized, and CDO/SOC dressings were replaced by new material.

### *Outcomes*

The primary outcome included >10% of scar length reduction and %change in scar length at 4 weeks compared to baseline. The secondary outcome included %change in SatO2, a novel parameter widely assessed particularly among patients with chronic dermal lesions.[5-8] For scar reduction and SatO2 assessment, a validated non-invasive near-infrared (NIR) camera (Snapshot NIR, KENT Imaging Inc., Calgary, AB, Can) that objectively measures length of wounds and detects real-time approximate value of SatO2 level in superficial tissue was used. All measurements were obtained before placement of SOC or CDO during each visit. Scar length was measured by tracing the incision linear perimeter from end to end and SatO2 was measured by tracing a 1-cm diameter around the wound length using the ROI Measurement Tool (SnapShot NIR Viewer, KENT Imaging Inc., Calgary, AB, CAN). To reduce the bias of wound length and SatO2 measurements, all wounds were measured using an identical tracing technique.

### *Feasibility of therapy*

Device acceptability in the IG was assessed with a technology acceptance model (TAM)[29] questionnaire tailored for the purpose of this study (Table I) during each follow up visit. Moreover, quality of life questionnaires such as PROMIS (physical and emotional status), PSQI (sleep quality) and VAS (pain) were repeatedly assessed at the end of the study period.

### *Sample size justification*

This is a feasibility and acceptability study in which the effectiveness of a CDO dressing in patients undergoing cervicotomy was examined in the context of a proof of concept RCT. To our knowledge, there is no prior study exploring the benefit of CDO in reducing scar length, thus, we estimated the sample size based on Song et al study,[30] in which the effectiveness of hyperbaric oxygen therapy (HBOT) to reduce keloid recurrence after upper chest surgical excision was assessed among 240 patients. In this study, scar scale score was reduced significantly in the group who received hyperbaric oxygen therapy compared to the control group, representing a very large effect size (Cohen effect size, $d = 2.12$). We assumed a similar effect size to examine the benefit of CDO in reducing scar length. By assuming a statistical power of 80%, alpha of 5%, an attrition rate of 10%, and 2-tailed t-test, the minimum sample size required to observe change in scar length is estimated to be 6 subjects per group. In this study, we recruited 21 subjects (IG = 12; CG = 9).

### *Statistical analysis*

All continuous data was presented as mean ± standard error, and categorical data was expressed as percentage. Independent samples t tests were used to examine mean differences between group on continuous demographic and clinical data. Analysis of Chi-square was used to assess comparison of categorical demographics, clinical data, and proportion of patients achieving >10% of scar reduction. All scores were normally distributed ($P > 0.05$), as assessed by Shapiro–Wilk's test of normality. If the assumption of normality was violated, logarithmic transformation was performed. Furthermore, the assumption of homogeneity of variance across groups was verified using the Levene's Test. A one-way analysis of covariance (ANCOVA) was conducted to assess the %change in scar length and SatO2 between groups with and without adjusting for potential confounders (e.g., age). Moreover, a sub-sample

**Table 1 – Device acceptability survey developed based on Technology Acceptance Model (TAM) to evaluate perceived usefulness, perceived ease of use, and attitude toward using the continuous diffusion of oxygen device.**

| # | TAM Item | | Strongly Agree (7) | Agree (6) | Somewhat Agree (5) | Neutral (4) | Somewhat Disagree (3) | Disagree (2) | Strongly Disagree (1) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Perceived Usefulness | I felt less pain during the day/night | | | | | | | |
| 2 | | Caused me physical pain | | | | | | | |
| 3 | | I felt less swollen | | | | | | | |
| 4 | | Caused me to trip more | | | | | | | |
| 5 | Perceived Ease of Use | It was easy to carry during daily activities | | | | | | | |
| 6 | | Charging was easy | | | | | | | |
| 7 | | Showering was easy | | | | | | | |
| 8 | | Was comfortable to wear | | | | | | | |
| 9 | Attitude Toward Using | Has been a pleasant experience | | | | | | | |
| 10 | | I would wear it again | | | | | | | |
| 11 | | I would recommend to a friend | | | | | | | |

A Likert scale was used to score each response. Except for item #2, each answer was scored from 7 to 1, respectively, from strongly agree to strongly disagree. For item #2, a similar score on reversed order was used.

of the participants depending on thyroid and parathyroid disease was also analyzed in the same fashion. Cohen's d effect size was calculated to assess the magnitude of difference between each group. Values in the range from 0.20 to 0.49 indicate small, within 0.50 and 0.79 indicate medium, and the range from 0.80 to 1.29 indicate large effects.[31] Statistical significance was defined as $P < 0.05$. All statistical analyses were performed using IBM SPSS Statistics 24 (IBM, Chicago, IL, USA).

## Results

Twenty-one patients were recruited (Age: 53 ± 16 years; 90% female; CG=9, IG=12), however five were lost to follow-up due to non-compliance (n=4) or discomfort (n=1), leaving a total of sixteen patients (Figure 2). Demographics and clinical data are summarized in Table II. The CG participants were younger (CG=44.3 ± 6.6 versus IG=64 ± 2.6 years old, d=1.54, p=0.024) than the IG participants. All other baseline demographics and clinical characteristics were not significantly different between groups.

### *Scar length*

At 4 weeks, 88.8% of the IG significantly achieved >10% of scar reduction compared to the CG (28.5%, d = 0.48, $P = 0.049$). Furthermore, the %change in scar length was log transformed to satisfy the assumption of normality. After this setting, the IG showed a trend of 40.4% smaller scar compared to the CG (15.7% ± 3.3% versus 11.2% ± 3.6%, [unadjusted: d = 0.68, $P = 0.20$]; [adjusted: d = 0.13, p = 0.72, Fig. 3A]), however difference was not significant.

A sub-analysis of the overall cohort was performed depending on patients' thyroid or parathyroid disease to evaluate wound healing under these two different conditions. The IG showed a significant effect for %change in scar reduction in patients with hyperthyroidism undergoing cervicotomy, surpassing the CG in 127% (IG=11.6% ± 0.6% versus CG = 5.1% ± 1.2%, [unadjusted: d = 2.96, $P = 0.009$, Fig.3B]; [adjusted: d = 1.1, $P = 0.098$]). Additionally, the proportion of patients achieving >10% of scar reduction in this sub-group was significantly higher (IG = 100%, CG = 0%, d = 0.82, $P = 0.008$). On the other hand, no effect was seen in patients with hyperparathyroidism undergoing cervicotomy (IG = 17.7% ± 4.8% versus CG = 19.2 ± 5.7%, [unadjusted: d = 0.13, $P = 0.854$, Fig. 3C]; [adjusted: d = 0.07, $P = 0.9$]), nor when evaluating the proportion of patients achieving >10% of scar reduction (IG = 66.7%, CG = 66.7%, d = 0.82, $P = 1.0$).

### *SatO2*

Tissue SatO2 showed no significant differences between groups (IG = 2.6% ± 4.7% versus CG = 9% ± 12.4%, [unadjusted: d = 0.28, $P = 0.64$]; [adjusted: d = 0.07, $P = 0.91$]). When sub-analyzing patients depending on illness, there were no significant differences for the thyroid (IG = 9.4% ± 4.3%, CG = 10.6% ± 19.9%, [unadjusted: d = 0.05, $P = 0.97$]; [adjusted: d = 0.61, $P = 0.61$]) or parathyroid (IG = -0.7% ± 6.1% versus CG = 6.9 ± 16.7%, [unadjusted: d = 0.65, $P = 0.4$]; [adjusted: d = 0.9, p = 0.33]) sub-groups.

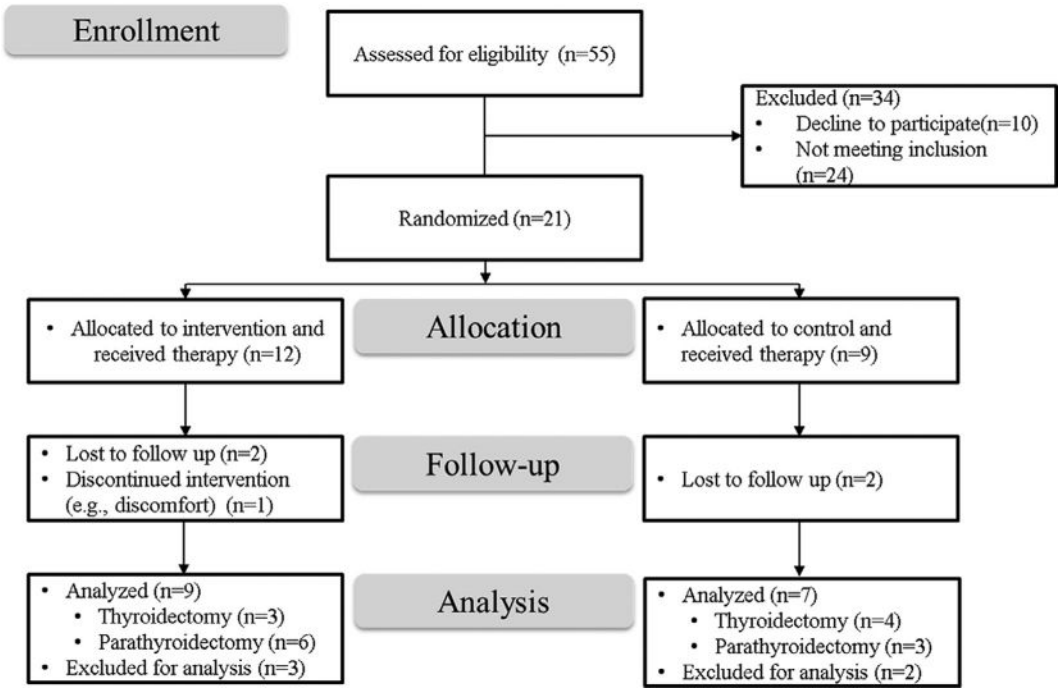


**Fig. 2 – Consort chart diagram of the present study.**

**Table 2 – Patient demographics and clinical characteristics.**

| Variable | Control($n = 7$) | Intervention($n = 9$) | *P*-value |
|---|---|---|---|
| Age (years) | 44.3 ± 6.6 | 64.0 ± 2.6 | 0.024 |
| BMI (kg/m$^2$) | 32.7 ± 2.9 | 32.5 ± 2.6 | 0.96 |
| Female (n) | 7 (100) | 7 (77.7) | 0.47 |
| Thyroid disease | 4 (57.1) | 3 (33.3) | 0.61 |
| Parathyroid disease | 3 (42.8) | 6 (66.7) | 0.61 |
| Diabetes | 2 (22.2) | 5 (41.7) | 0.36 |
| Hypertension | 4 (57.1) | 6 (66.7) | 1 |
| Dyslipidemia | 2 (28.5) | 3 (33.3) | 1 |
| Chronic Kidney Disease | 1 (14.3) | 1 (11.1) | 0.85 |
| Depression | 0 | 2 (22.2) | 0.18 |
| Frail | 1 (14.2) | 2 (22.2) | 1 |
| Daily prescribed meds (no.) | 5 ± 4.5 | 6.5 ± 3.5 | 0.95 |
| Glucose, mg/dL | 105.3 ± 8.3 | 113.3 ± 8.9 | 0.55 |
| Cognitive function (MoCA score) | 25.5 ± 0.6 | 23.6 ± 1.7 | 0.5 |
| Sleep quality (PSQI score) | 6.6 ± 1.9 | 8.0 ± 1.4 | 0.56 |
| Global Health (PROMIS score) | 29.3 ± 1.8 | 33.4 ± 1.8 | 0.10 |
| Wound length, cm | 5.2 ± 0.6 | 4.4 ± 0.4 | 0.31 |
| Wound SatO2, % | 59.3 ± 3.1 | 60.6 ± 2.1 | 0.73 |

Values are presented as mean ± standard deviation or *n* (%). BMI = body mass index; CKD = chronic kidney disease; MoCA = montreal cognitive assessment; PSQI = pittsburgh sleep quality index; PROMIS = patient-reported outcomes measurement information system; SatO2 = tissue oxygen saturation.

### *Feasibility of therapy*

No functional device problem or related adverse events (i.e., pain, rash or systemic toxicity) were reported. Among the IG, 91.6% (11/12) of the patients were able to complete the TAM survey (Table I) at their last follow up visit. Patient agreement showed 73% of perceived usefulness (Item #1: 80%; #2: 79.2%; #3: 85.7%, and #4: 46.7%), 74.1% perceived ease of use (Item #5: 76.6%; #6: 91.4%; #7: 61%, and #8: 67.5%), and 84% attitude toward using (Item #9: 80.5%; #10: 84.4%; and #11: 87%). The

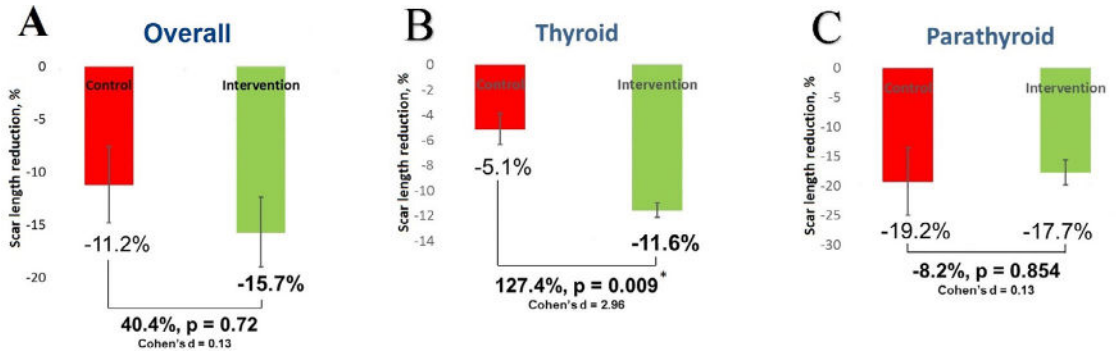


**Fig. 3 – Overall and sub-sample %change in scar length. Panel (A) Overall comparison of %change in scar length adjusted to age. (B) Thyroid disease patient sub-sample comparison of unadjusted (due to low sample size) %change in scar length. (C) Parathyroid disease patient sub-sample comparison of unadjusted (due to low sample size) %change in scar length. Results correspond to 4 weeks of post-operative care. * Statistically significant.**

PROMIS (d = 0.65, P = 0.24), PSQI (d = -0.15, P = 0.77), and VAS (d = 0.46, P = 0.40) questionnaires did not show significant differences between groups at the end of the study period.

## Discussion

Oxygen is an essential requirement for mediating wound healing.[32] Pre-clinical studies have demonstrated its effect at short (vasoconstriction, edema reduction, phagocyte activation) and long (angio, osteo, and collagenogenesis) term therapy.[33-36] When applied topically, oxygen reaches wounds more readily,[37] reducing the risk of post-operative skin infections[38] and local tissue ischemia.[39] However, most evidence for wound treatment has been reported aside from the anterior neck area,[21, 40, 41] and the effect of topical oxygen therapy post-thyroid/parathyroid surgery has not been widely assessed. We sought to examine the effect of CDO among patients in regards to scar length and tissue oxygenation.

Benefits for neck surgery have been observed with supplemental oxygen therapy, however the literature accounts for hyperbaric oxygenation reviews.[42-45] Moreover, there is only one publication (case report) demonstrating the efficacy of topical oxygen in the (lateral) neck region.[46] On behalf of these limitations, we included an objective modality to evaluate scar reduction in a RCT. After one month of CDO therapy, a significant proportion of patients presenting >10% in scar length reduction in addition to a 40.4% lower trend for wound size defined the use of topical oxygen (Fig. 3A), even though the IG was significantly older and given the fact that oxygen epidermal levels decline with age (50% deficit at 40 years).[47] These results align with previous retrospective studies using topical oxygen as an adjunctive therapy in aiding complex wounds.[48-50]

In addition, after the dichotomization of the IG into thyroid and parathyroid disease, the thyroid sub-group under CDO therapy showed a significant reduction in scar length with a very large effect size without adjusting age as a covariate due to the low sample size (Fig. 3B). It is known that hyperthyroidism increases wound healing[51-55] and after altering the glands' metabolism by resection, scar remodeling could have been stabilized back to normal conditions. Therefore, showing benefit to those who underwent CDO therapy (Fig. 4A). This was also evident given the fact that all the patients in the thyroidectomy sub-group undergoing CDO resulted in >10% in scar reduction, opposite to the CG. However, it is uncertain the time of elimination of circulating thyroid hormone after undergoing partial or total thyroidectomy, thus, this finding could be coincidental. On the contrary, limited data indicates a parathyroidectomy has potential to improve wound healing after removing the gland(s),[56-58] suggesting a mechanism that could have been reflected in the fast and increased similar reduction of wound size in both sub-groups (Fig. 3C and 4B). Even though the effect size for this comparison was very large, the small sub-sample population is still a limitation, thus, conclusions made for this observation are uncertain. More patients are needed to confirm this statement.

In wounds, topical oxygen increases SatO2 through ROS stimulation that eventually increases angiogenesis.[59-63] However, tissue hypoxia has also found to initiate angiogenesis in acute stages,[60] meaning that neovascularization moves toward hypoxic regions.[64] In our study, whether using or not CDO, there was no significant differences for tissue perfusion between groups, suggesting that the main factor for cervicotomy length reduction might not rely in the level of angiogenesis. However, since collagen synthesis and fibroblasts deposition are enhanced by topical oxygenation,[65] migration of these factors might not have been impaired in our study. This could have reduced scar length in the IG (Fig. 4C), but ultimately, tissue perfusion did not show any different pattern than the CG; both somewhat improved. Whether competition for epithelial enhancement or the not much different angiogenesis effect by CDO showed contrasting results, this must be formally investigated in cervicotomies before conclusions can be drawn.[64] Other important factors for SatO2 evaluation were the weekly manipulation of dressing changes in the IG, or the younger CG age which positively influences tissue oxygenation as previously mentioned.

One important observation was the quality of life and device acceptability assessments. Even though perceived useful-

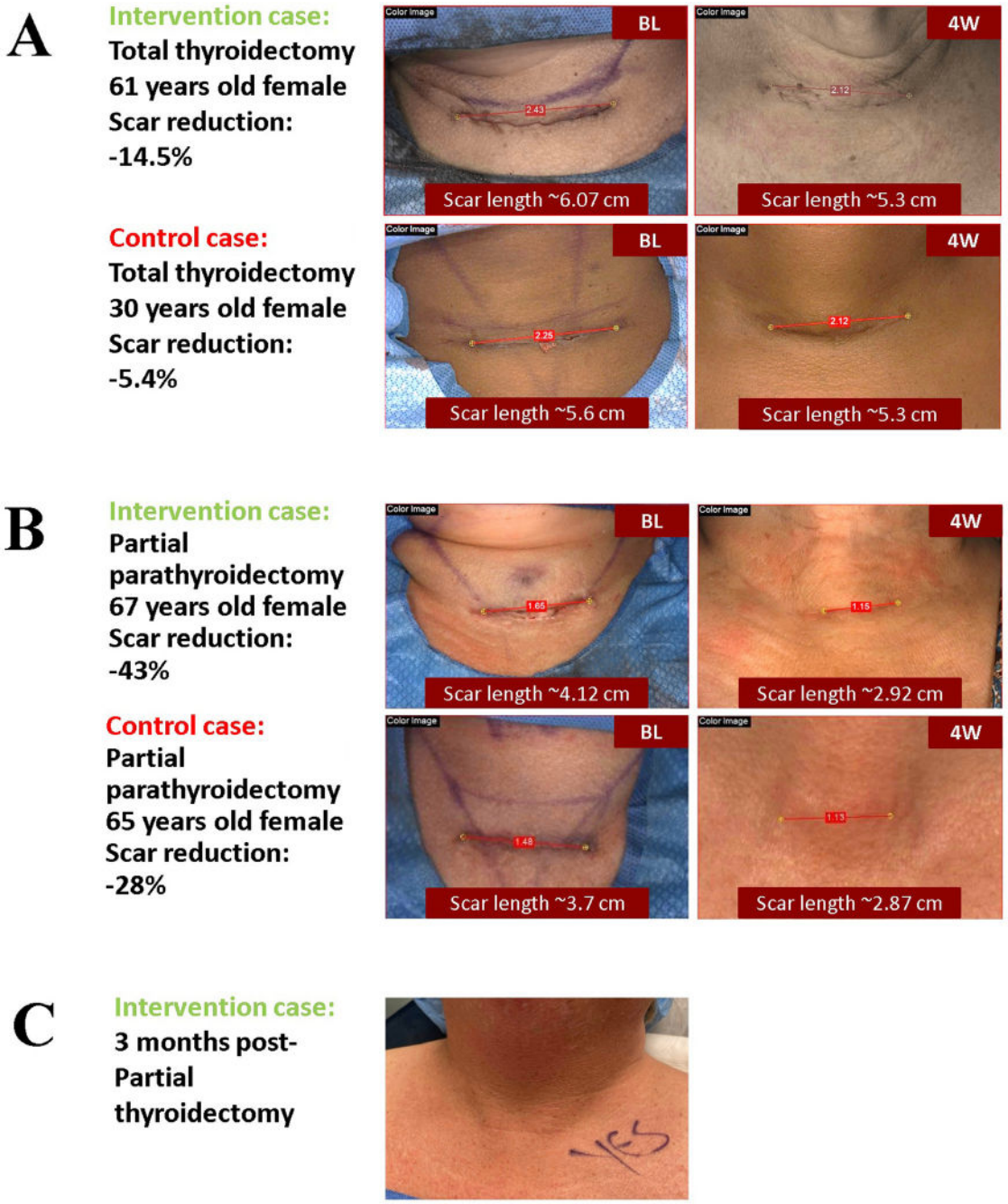


**Fig. 4 – Typical cases with and without continuous diffusion of oxygen adjunct therapy depending on type of disease. (A) 2-case comparison of patients undergoing thyroidectomy with and without CDO therapy. (B) 2-case comparison of patients undergoing parathyroidectomy with and without CDO therapy. (C) Intervention case of a partial thyroidectomy in a 58 years old female with history of diabetes mellitus and follicular thyroid carcinoma after 3 months post-cervicotomy. Despite the high comorbidities, scar formation is barely seen.**

ness and ease of use were around 75% of agreement in the IG, attitude toward using was promising with an 84%. Moreover, the global health, sleep, and pain questionnaires did not show significant differences between groups at the end of the study. Most issues were related to external dressings or latex allergy that could be replaced or improved for future treatments. CDO itself did not show harmful signs, irritation, or systemic toxicity.

### *Limitations*

The main limitation of this study is the sample size. Priori size justification was performed for the entire cohort, but not for the sub-samples. The software modality for tracing wounds was linear and all wounds were measured from end to end regardless of shape. There was a 10ml pre-surgical 0.25% bupivacaine injection with 1:100,000 epinephrine in the incision site

that could have been influenced SatO2 baseline levels due to vasoconstriction. In addition, some patients in the IG reported soft rash due to the Tegaderm™ Film, which was immediately replaced for a non-latex dressing. This factor could have also affected the area of SatO2 evaluation due to the altered skin conditions and/or dressing manipulation. A histological analysis would be needed to evaluate the truly rate of angiogenesis in the neck area after a cervicotomy. Moreover, width and wound height, as well as aesthetic outcomes were not included, something important to assess in future long-term studies. Replacement for new dressings were done in a weekly basis, and all patients were advised to maintain the dressing intact. However, due to the reported patient comfortability, it is difficult to ascertain if continuous flow was stopped/resumed at some point. This study is still ongoing, and given the observations from the sub-sample of patients undergoing thyroidectomy, the expansion will further include only this subpopulation. Future studies by specific type of disease are warrant to empower the implications of the influence of CDO for thyroid- or parathyroidectomy.

## Conclusion

To the best of our knowledge, this is the first RCT to highlight the efficacy of CDO to reduce SF of the wound site for patients following cervicotomy for thyroid or parathyroid disease. Results suggest that advanced dressing using CDO may improve wound healing showing better outcomes for scar visualization in patients undergoing thyroidectomy. We speculate that reduced scar in the IG is due to the early and increased migration of remodeling agents (i.e., fibroblasts, collagen), in response to CDO. However, this should be demonstrated in histological studies for anterior neck surgery. This modality of therapy might be feasible and does not affect the quality of life of patients undergoing anterior neck surgery. Nonetheless, a larger sample is required to validate these observations.

## Author contributions

Conception and design: BN, JS, AZ; Analysis and interpretation: BN, JS, AZ; Data collection: AZ; Writing article: AZ, AP; Critical revision of the article: BN, JS; Final approval of the article: BN, JS; Statistical analysis: RM; Overall responsibility: BN.

## Disclosure

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