Research Square

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Efficacy of early postoperative ON101 application for lower- extremity fracture incisions: a prospective evaluator-blinded controlled study of scar quality and digital-clinical concordance

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Research Article

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Abstract

Background

Postoperative scars after lower-extremity fracture fixation endure high tension, where excessive scarring can restrict periarticular mobility. While the 2002 International Clinical Recommendations on Scar Management emphasize early prevention, conventional silicone products require complete epithelialization before use. Conversely, ON101 is a topical formulation. The formulation helps to maintain the wound moist environment, and the moist wound environment is conducive for wound healing. This profile suggests potential for earlier intervention. We evaluated whether initiating ON101 during the early postoperative repair phase improves subsequent wound healing and scar maturation.

Methods

This prospective, evaluator-blinded, controlled study enrolled 30 adults undergoing open reduction and internal fixation for lower-extremity fractures. Patients received once-daily topical ON101 (n = 20) or standard care (n = 10), initiated within 3 days postoperatively before complete epithelialization, and continued for 16 weeks. Blinded clinicians assessed scar maturation using the Vancouver Scar Scale (VSS). Standardized photographs were quantitatively analyzed using CIELab color parameters and gray-level co-occurrence matrix (GLCM) texture features.

Results

All 30 participants completed the 16-week treatment. The ON101 group demonstrated greater improvement in total VSS scores from the initial evaluable assessment to Week 16 than controls (51.22% vs. 15.10%, $p < 0.001$). ON101 also yielded significantly greater improvements in vascularity (64.98% vs. 28.33%, $p < 0.001$), pliability (49.35% vs. -2.08%, $p = 0.001$), and height (44.32% vs. -16.67%, $p < 0.001$). Objective image analysis detected treatment-associated differences in color and texture by Weeks 2–16, preceding clinical VSS divergence. No treatment-related adverse events or wound complications were observed.

Conclusions

From our study, early intervention before epithelialization of orthopedic surgical wound for trauma is associated with more favorable scar maturation in both subjective and objective evaluation tools. While establishing robust improvements in early scar morphology, larger randomized trials are warranted to confirm definitive functional benefits.

Trial registration

ClinicalTrials.gov, NCT07854470. Retrospectively registered and publicly posted on 2 October 2026.

Background

Orthopedic fracture surgery frequently requires incisions that traverse traumatized soft tissue and extend through the fascia and muscle to the fracture site. When located adjacent to lower-extremity joints, these wounds are continuously exposed to high tension, shear, and repetitive movement during postoperative rehabilitation. Consequently, postoperative scarring in orthopedics has clinical implications beyond cosmesis; excessive scar thickening, tissue adhesion, and joint contracture can restrict periarticular mobility, contribute to pain, and severely impair functional recovery [1]. Furthermore, Asian populations are particularly susceptible to postoperative hypertrophic scarring. Studies in Chinese orthopedic patients report a high incidence of hypertrophic scars following joint surgeries, particularly around the knee, emphasizing the critical need for robust preventive strategies in this demographic [2, 3].

International clinical recommendations on scar management strongly emphasize that early prevention of hypertrophic scars is more efficient than treating an established pathological scar [4]. However, achieving true early prevention remains clinically challenging. Most scar management products are intended for application on fully epithelialized wounds, as their efficacy relies on an intact skin surface (e.g., silicone sheets or topical gels). Their primary role is to maintain hydration and support barrier function rather than actively modulate the wound microenvironment [5]. Premature application to open or exudative wounds may increase the risk of infection, cause tissue maceration, and potentially delay wound healing [6–8]. Consequently, a critical therapeutic gap exists during the early postoperative repair phase, when inflammation, extracellular-matrix deposition, and other biological processes that ultimately determine scar formation remain amenable to intervention. At this stage, orthopedic surgeons have few therapeutic options to actively modulate these processes before irreversible scar architecture becomes established. Therefore, interventions that can be safely initiated during this biologically active phase represent a major unmet clinical need.

To bridge this therapeutic gap, ON101 emerges as a promising candidate. ON101 is a standardized topical formulation containing defined fractions derived from *Plectranthus amboinicus* and *Centella asiatica* [9–11]. The formulation helps to maintain the wound moist environment, and the moist wound environment is conducive for wound healing [12, 13]. Unlike conventional products that depend merely on physical occlusion after epidermal closure, ON101's intrinsic wound-healing properties allow it to be safely initiated on acute surgical wounds during the active, early repair phase.

Therefore, this prospective, evaluator-blinded, controlled study aimed to evaluate whether early ON101 intervention—initiated within three days postoperatively before complete wound closure—could overcome current limitations in orthopedic scar management. Because no available scar scale was developed specifically for orthopedic wounds, we combined clinician-rated assessments (Vancouver Scar Scale, VSS) with a novel quantitative digital photography analysis system to objectively capture subtle longitudinal changes in scar color and texture. We hypothesized that early ON101 intervention would optimize the early tissue repair phase and improve subsequent scar maturation, particularly in periarticular wounds. To our knowledge, this is the first prospective orthopedic study to evaluate ON101 during the early repair phase before complete epithelialization, aiming to fulfill the early prevention paradigm championed by international guidelines by intercepting scar worsening from the outset.

Methods

This study was designed as a prospective, evaluator-blinded, controlled study to investigate the effects of ON101 cream on post-surgical scarring following open reduction and internal fixation of lower extremity fractures (from hip to ankle). From January 2023 to October 2024, patients were enrolled at a single tertiary-referral medical center, where all surgeries were performed by the same orthopedic surgeon to ensure consistency in surgical technique and postoperative care. Eligible participants were adults aged 18–65 years who had undergone primary wound closure for clean surgical incisions resulting from lower extremity or hip fracture surgeries, with ON101 application within three days postoperatively. All participants provided written informed consent and were required to comply with the study protocol. Exclusion criteria included diabetes mellitus, pregnancy or lactation, ongoing systemic corticosteroid, radiation, or immunosuppressive therapy, known or suspected allergies to the study product, HIV infection, or any clinically significant condition that, in the investigator's judgment, could interfere with wound healing or study compliance. Thirty participants were classified into two groups. Patients in the treatment group received topical ON101 cream (n = 20) starting at V2, whereas those in the control group (n = 10) received standard care alone. Both treatments were applied once daily for 16 weeks. The assessment time points were defined as follows: V2 (Day 0, baseline), V3 (Week 1), V4 (Week 2), V5 (Week 4), V6 (Week 8), V7 (Week 12), and V8 (Week 16). Clinical scar assessments were conducted and photographed at each time point, using both subjective and objective methods (Fig. 1A).

Subjective evaluation employed the Vancouver Scar Scale (VSS), which assesses pigmentation, vascularity, pliability, and scar height. Because reliable assessment of height and pliability required suture removal and sufficient wound stabilization, VSS scoring began at V4 (Week 2) and continued through V8. Three independent evaluators performed the VSS scoring. Blinding of outcome assessors and data analysts was maintained throughout the study using standardized photographic protocols and anonymized images to ensure the assessors were unaware of patient identity, treatment group, and time point. Although the VSS was originally developed for burn scars, it is among the most widely used scar instruments and has been applied successfully in total hip arthroplasty, total knee arthroplasty, and limb reconstruction studies [1, 4].

For objective evaluation, a quantitative digital photography analysis was performed. At each time point from V4 to V8, four standardized photographs (anterior-posterior views) of each scar site were taken using a Canon EOS 850D with maximum resolution settings and standard procedures (e.g., the camera-to-subject distance was fixed at 30 cm). Image data were processed using MATLAB. The image analysis algorithm (Fig. 1B) segmented the scar region from the surrounding skin and extracted quantitative features of color and texture. The baseline image at V4 served as reference. Scar contrast was expressed as delta (Δ), defined as the difference between scar and adjacent skin. Additionally, a difference ratio (Δ ratio = Δ (scar–skin)/skin) was calculated, where higher values indicated more prominent scar features—either in color (e.g., discoloration) or texture (e.g., elevation or depression).

Color analysis included both Hue and CIELab color spaces. Texture analysis was conducted using the Gray-Level Co-occurrence Matrix (GLCM), which captures the spatial relationship of pixel intensities to reflect visual roughness and directionality. Two second-order statistical features—dissimilarity and homogeneity—were extracted from the normalized GLCM (sum of elements = 1) to quantify scar-related texture changes. Dissimilarity measures the degree of difference between neighboring pixels. Higher values indicate greater gray-level variation between adjacent pixels, reflecting a coarser and more heterogeneous texture. Conversely, homogeneity measures the similarity between neighboring pixels. Higher values indicate a smoother and more uniform texture. Although these two features are generally inversely correlated, they are not exact opposites because they are derived using different mathematical formulations. These objective metrics provide quantifiable indicators of scar cosmesis, complementing clinical assessments. Further details regarding the digital photographic analysis can be found in our previous publication [14].

Statistical analysis

Descriptive statistics were used to summarize patient characteristics. Continuous variables (e.g., age) are expressed as mean ± standard deviation, and categorical variables (e.g., gender and trauma mechanism) are expressed as frequencies and percentages. Comparisons between the ON101 group and the control group were performed using the independent t-test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. VSS improvement was summarized as absolute gain and improvement ratio, calculated as (initial VSS - final VSS)/initial VSS. Statistical analyses were conducted using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was accepted at $p < 0.05$.

Ethical considerations

The research protocol (KSVGH22-CT11-16) was reviewed and approved by the Institutional Review Board. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent to participate was obtained from all participants. The study was retrospectively registered with ClinicalTrials.gov (NCT07854470); the registration was first submitted on 11 September 2026 and publicly posted on 2 October 2026.

Results

Patient and incision characteristics

Thirty participants were enrolled between April 2023 and August 2024, including 20 in the ON101 group and 10 in the control group. The study population comprised 19 men and 11 women, with a mean age of 40.0 ± 14.6 years (range, 21–65 years). All participants completed the 16-week follow-up and were included in the final analysis. Baseline demographic and clinical characteristics are summarized in Table 1.

Traffic accidents were the predominant mechanism of injury. Because several patients sustained fractures requiring surgical incisions at multiple anatomical sites, a total of 27 evaluable incision sites in the ON101 group and 12 in the control group were included in the analysis. Incision locations comprised the joint (hip, knee and ankle) and non-joint (thigh and lower leg) region. Periarticular incisions represented 85.2% and 75.0% of incision sites in the ON101 and control groups, respectively. The mean incision length was comparable between groups (9.82 cm vs. 10.23 cm), with no significant differences ($p = 0.787$) observed either overall or across anatomical-site categories. Participants in both groups were enrolled at a mean of approximately 2 days after surgery and subsequently received either ON101 or standard of care (SOC). The interval from treatment initiation to suture removal was identical between the two groups, averaging approximately 9 days. The distribution of orthopedic fixation procedures, including plating, nailing, and screwing, was comparable between groups ($p = 0.861$). Baseline demographic, surgical, and wound characteristics, including wound closure techniques, incision characteristics, and time to suture removal, were well balanced between the two groups, indicating that postoperative wound healing conditions were comparable and supporting the validity of subsequent between-group comparisons of scar outcomes. In accordance with Taiwan's National Health Insurance practice, the average postoperative hospital stay was approximately 5 days in both groups. No treatment-related infection, allergic reaction, wound dehiscence, or other postoperative wound complications were observed during the study. Two participants in the ON101 group developed transient postoperative erythema considered consistent with surgery-related inflammation. Both events resolved spontaneously without treatment discontinuation or sequelae.

Table 1
Demographic, surgical, and incision characteristics of the study participants.

Characteristics	ON101 group (N = 20)	Control group (N = 10)	p value
	n (%)	n (%)	
Gender			
Male	15 (75%)	4 (40%)	0.108
Female	5 (25%)	6 (60%)	
Age			
Mean (SD), years	39 (13.81)	42 (14.47)	0.308
18–25	3 (15%)	3 (30%)	0.335
26–45	11 (55%)	2 (20%)	
46–65	6 (30%)	5 (50%)	
Trauma mechanism			
Fallen	5 (25%)	2 (20%)	0.526
Car accident	13 (65%)	8 (80%)	
Heavy pressure	2 (10%)	0 (0%)	
Lower limb trauma			
Left	10 (50%)	7 (70%)	0.440
Right	10 (50%)	3 (30%)	
Fracture location			
Hip	6 (23.1%)	2 (15.3%)	0.323
Femoral	2 (7.7%)	3 (23.1%)	
Patella	0 (0%)	1 (7.7%)	
Tibial plateau	6 (23.1%)	0 (0%)	
Fibula	5 (19.2%)	3 (23.1%)	
Tibial	5 (19.2%)	3 (23.1%)	
Ankle	2 (7.7%)	1 (7.7%)	
Suture location			

Characteristics	ON101 group (N = 20)	Control group (N = 10)	p value
	n (%)	n (%)	
Gender			
Joint	23 (85.2%)	9 (75.0%)	0.654
Non-joint	4 (14.8%)	3 (25.0%)	
Suture length			
Mean (SD), cm	9.82 (4.56)	10.23 (3.66)	0.787
Surgical method			
Plating	7 (35%)	3 (30%)	0.861
Nailing	12 (60%)	6 (60%)	
Screwing	1 (5%)	1 (10%)	
Days from surgery to enrollment			
Mean (SD), days	2 (0.83)	2 (0.94)	0.324
Time from enrollment to suture removal			
Mean (SD), days	9 (2.04)	9 (2.86)	0.494
Length of hospitalization stay			
Mean (SD), days	5 (1.76)	5 (2.34)	0.755

Note. Data are presented as n (%) unless otherwise indicated. Participant-level and incision-level characteristics are reported according to the corresponding analysis unit. SD, standard deviation.

Representative serial photographs (Fig. 2) consistently demonstrated earlier reduction of erythema, progressive scar flattening, and progressive convergence of scar appearance toward the surrounding skin in the ON101 group. Representative cases included both hip and ankle incisions following different injury mechanisms (traffic accident and fall), illustrating that similar trends in scar improvement were observed across representative periarticular orthopedic wounds. At the 16-week assessment, ON101-treated scars exhibited less erythema, reduced elevation, and greater resemblance in color and surface appearance to the surrounding skin than control scars. These visual findings were concordant with both clinician-rated VSS improvement and quantitative digital image analysis.

Clinician-rated scar assessment

Three blinded clinicians independently evaluated scar maturation using the Vancouver Scar Scale (VSS) from V4 (Week 2) through V8 (Week 16). At the Week 2 baseline assessment, no statistically significant between-group differences were observed in total VSS score or in the individual domains of pigmentation, vascularity, pliability, and height. Over the subsequent follow-up period, the ON101 group demonstrated greater reductions in total VSS score and more favorable changes across the individual VSS domains than the control group. Between-group separation became clinically apparent from approximately Week 4 onward, particularly for vascularity, pliability, and height (Fig. 3).

The VSS improvement ratio was calculated as [(initial VSS –final VSS) / initial VSS]*100%—further demonstrated the superiority of the ON101 group over the control group. As shown in Table 2, the mean improvement ratio for total VSS score was 51.22% in the ON101 group compared with 15.10% in the control group ($p < 0.001$). The corresponding improvement ratios were 64.98% versus 28.33% for vascularity ($p < 0.001$), 49.35% versus − 2.08% for pliability ($p = 0.001$), and 44.32% versus − 16.67% for height ($p < 0.001$). Pigmentation also showed a numerically greater improvement in the ON101 group than in the control group (40.93% vs. 19.96%); however, the between-group difference was not statistically significant ($p = 0.421$). These findings indicate that the principal clinician-rated differences were observed in scar vascularity, pliability, height, and total VSS score, whereas the improvement in pigmentation did not reach statistical significance in the gain-ratio analysis.

Table 2
Changes and improvement ratios in Vancouver Scar Scale scores from Week 2 to Week 16.

	VSS				
	Initial (V4)	Final (V8)	Gain (Initial-Final)	Ratio (Initial-Final)/Initial	p value
Total					
ON101 group	4.45 (1.139)	2.17 (1.192)	2.28	51.22%	< 0.001
Control group	4.81 (0.602)	4.08 (1.339)	0.73	15.10%	
Pigmentation					
ON101 group	1.82 (0.654)	1.07 (0.519)	0.74	40.93%	0.421
Control group	2.05 (0.384)	1.64 (0.543)	0.41	19.96%	
Vascularity					
ON101 group	1.73 (0.735)	0.60 (0.585)	1.12	64.98%	< 0.001
Control group	1.67 (0.483)	1.19 (0.668)	0.47	28.33%	
Pliability					
ON101 group	1.68 (0.646)	0.85 (0.362)	0.83	49.35%	0.001
Control group	1.71 (0.488)	1.75 (0.452)	-0.04	-2.08%	
Height					
ON101 group	0.91 (0.455)	0.51 (0.615)	0.40	44.32%	< 0.001
Control group	1.10 (0.436)	1.28 (0.815)	-0.18	-16.67%	

Note. Values are presented as mean (SD). Gain was calculated as the V4 (Week 2) value minus the V8 (Week 16) value; improvement ratio was calculated as gain divided by the V4 (Week 2) value. SD, standard deviation; VSS, Vancouver Scar Scale.

Quantitative digital color analysis

Quantitative digital image analysis provided objective measurements of longitudinal changes in scar color relative to adjacent skin. A significant between-group difference in CIELab L* was detected as early as V4 (Week 2) ($p < 0.001$), indicating an earlier change in scar lightness in the ON101 group (Fig. 4D). During follow-up, the scar-to-skin differences in the CIELab a* and b* components also decreased more prominently in the ON101 group, indicating progressive convergence toward the color characteristics of adjacent skin. Statistically significant between-group differences were observed in a* ($p < 0.05$) and b* ($p < 0.01$) during follow-up (Fig. 4E and F).

Because a lower a* difference indicates reduced scar erythema and a lower scar-to-skin color difference reflects closer approximation to surrounding skin, these trends were consistent with earlier normalization of scar color in the ON101 group.

Quantitative digital texture analysis

Scar texture was quantified using gray-level co-occurrence matrix (GLCM)-derived dissimilarity and homogeneity parameters. At V5 (Week 4), dissimilarity was also significantly reduced in the ON101 group ($p = 0.003$), reflecting a smaller textural difference between the scar and adjacent skin. At V4 (Week 2), the ON101 group showed significantly greater improvement in homogeneity than the control group ($p = 0.002$), indicating a more uniform surface pattern (Fig. 4A and B). At the final V8 assessment (Week 16), both dissimilarity and homogeneity differed significantly between groups (both $p < 0.001$). ON101-treated scars showed lower dissimilarity and greater homogeneity, indicating a smoother and more spatially uniform scar surface.

Euclidean distances in the RGB color space were calculated using the red, green, and blue coordinates to quantify color differences between the ON101-treated and control groups (Fig. 4C). The RGB analysis demonstrated significant differences between the two groups. However, because the RGB color space is not perceptually uniform, numerical color differences do not necessarily correspond to the visual differences perceived by the human eye. Therefore, a more perceptually relevant color analysis was further performed using the CIELab color space. Color characteristics were subsequently quantified using the CIELab color space by analyzing the L*, a*, and b* parameters, calculating the corresponding difference ratios, and evaluating their temporal changes (Fig. 4D–F). Compared with the control group, the ON101-treated group demonstrated a significantly lower L* difference ratio at Week 16 ($p < 0.001$), indicating reduced hyperpigmentation and a color closer to the surrounding normal skin. In addition, the ON101-treated group showed significantly lower a* and b* difference ratios by the end of the study (a*: $p < 0.001$; b*: $p < 0.001$), indicating reduced red-green and blue-yellow color differences relative to the surrounding skin. These findings suggest that ON101 treatment promoted earlier scar maturation, as immature scars are typically characterized by increased erythema and darker pigmentation.

The digital assessments detected treatment-associated differences earlier than the clinician-rated VSS. Color differences were evident by Week 1, and texture differences by Week 2, whereas clear between-group separation in VSS scores emerged from approximately Week 4 onward. Overall, the image-derived color and texture measures demonstrated progressive convergence of ON101-treated scars toward the appearance and surface organization of adjacent skin.

Discussion

In this prospective, evaluator-blinded controlled study, initiation of ON101 within three days after lower-extremity fracture fixation was associated with more favorable early wound maturation. These findings are particularly relevant to orthopedic surgery because most evaluated incisions were located around

the hip, knee, or ankle, where wounds are continuously exposed to mechanical tension, repetitive movement, and shear stress during postoperative rehabilitation. Scar pliability and scar height are therefore not merely cosmetic outcomes in orthopedic surgery. Around mobile joints, excessive scar stiffness and hypertrophy may increase tissue tethering, restrict soft-tissue gliding, and potentially interfere with postoperative rehabilitation and functional recovery. Approximately 82% of the evaluated incisions in this study involved the hip, knee, or ankle, providing a clinically meaningful setting in which to evaluate early scar-modulating interventions. Although joint range of motion and functional outcomes were not directly assessed, the significant improvements observed in scar pliability and height suggest potential clinical benefits beyond scar appearance. A recent systematic review of orthopedic scar assessment similarly emphasized the importance of objective scar evaluation and highlighted the need for clinically meaningful outcome measures in postoperative orthopedic patients [1].

The need for improved scar management may be particularly important in Asian populations. Earlier research in Chinese orthopedic patients reported frequent postoperative hypertrophic scar features, including increased thickness, erythema, pain, and pruritus, with particularly prominent scarring near the knee [2]. More recently, hypertrophic scars were reported in 33.6% of Chinese patients after total hip or knee arthroplasty despite advances in surgical technique, wound closure, and postoperative care [3]. Differences in assessment timing, patient age, surgical procedures, and scar definitions may explain variation in the reported prevalence. Nevertheless, these studies consistently indicate that unfavorable postoperative scarring remains a clinically relevant problem in Chinese orthopedic populations and support investigation of interventions during the biologically active stages of wound healing.

Rather than treating scars after they become clinically apparent, early ON101 intervention shifts postoperative scar management toward earlier, moisture-based wound management during the repair phase. This strategy may be particularly valuable for periarticular orthopedic incisions, where preservation of scar quality may contribute to optimal rehabilitation and functional recovery. These findings support a paradigm shift from conventional post-epithelialization scar treatment toward earlier, moisture-retentive wound management during the critical repair phase. Whether these early morphological improvements translate into sustained reductions in pathological scar formation, preservation of joint mobility, improved scar-related symptoms, and better orthopedic outcomes should be confirmed in adequately powered randomized trials with longer follow-up.

The rationale for this strategy is supported by the established principles of moist wound healing. ON101 is a standardized topical formulation containing active fractions derived from *Plectranthus amboinicus* and *Centella asiatica*. This formulation helps to maintain the wound moist environment, and the moist wound environment is conducive for wound healing [12, 13]. Randomized clinical trials and real-world studies have also demonstrated wound-healing benefits in diabetic foot ulcers [9–11]. Although chronic diabetic ulcers and clean acute orthopedic incisions differ substantially in pathophysiology, these findings provide supporting evidence for evaluating early moisture-retentive wound management during postoperative wound repair.

Clinical evidence also supports an effect of ON101 on postoperative scar maturation. A previous prospective, placebo-controlled split-scar trial involving thyroidectomy and abdominal transverse incisions demonstrated significantly more favorable pigmentation, vascularity, pliability, scar height, patient satisfaction, and quantitative color and texture measurements on ON101-treated scar segments [14] The present study builds upon those observations by evaluating fracture-fixation incisions located predominantly around weight-bearing joints, where repetitive motion and mechanical loading create a more challenging healing environment. Despite the different anatomical sites and study designs, both prospective studies showed consistent treatment-associated improvements in scar maturation. The current results therefore broaden the clinical evidence from routine linear surgical incisions to orthopedic wounds subjected to greater biomechanical stress.

The within-participant comparison shown in Fig. 5 provides an illustrative example from the current clinical trial rather than an external case report. This participant was enrolled in the ON101 treatment group and sustained traumatic wounds requiring surgical management at two anatomical sites. At Week 16, the ON101-treated lower-leg incision showed more favorable scar maturation than the untreated upper-arm wound. Because this observation is descriptive and was not a prespecified paired comparison, it should not be interpreted as independent evidence of efficacy. Nevertheless, it visually complements the group-level findings while reducing the influence of interindividual factors such as age, genetic background, and intrinsic scar tendency.

Evidence from other functionally important wound settings is also relevant to the broader clinical hypothesis. A published post-marketing case described healing of a chronic anterior tendon-exposed diabetic foot ulcer after ON101 treatment, with preservation of ankle range of motion [15]. Although a single case cannot establish functional efficacy, it illustrates the potential importance of achieving durable soft-tissue coverage while maintaining tissue quality around a mobile joint. Collectively, the diabetic foot ulcer trials, prior postoperative scar trial, and current orthopedic investigation support early moisture-based wound management as a clinically supported strategy for improving tissue repair and subsequent scar maturation across different clinical settings. The present results are also consistent with the broader concept outlined in the FDA guidance for chronic cutaneous ulcers and burn wounds, which emphasizes that successful wound management should be evaluated not only by wound closure but also by the quality of healing, including scar appearance and preservation of function [16].

An additional strength of this study is the integration of blinded clinical assessment with standardized quantitative digital photography. Although conventional scar scales remain clinically useful, they rely on ordinal scoring and observer judgment. In contrast, CIELab color analysis and GLCM-derived texture features provided objective, quantitative longitudinal measurements of scar color and surface organization. Notably, quantitative imaging detected treatment-associated changes one to three weeks earlier than clinician-rated VSS, suggesting that digital image analysis may serve as an early-response biomarker for postoperative scar interventions. Earlier detection of treatment response may facilitate timely treatment optimization before clinically apparent scar abnormalities become established. Importantly, the concordance among blinded clinical assessment, quantitative image analysis, and serial

photographic findings strengthens the robustness of the present results. The consistent performance of this imaging approach in both the previous postoperative scar study and the current orthopedic investigation further supports its use as a complementary endpoint in future longitudinal and multicenter orthopedic trials. Nevertheless, quantitative imaging should complement, rather than replace, validated clinical scar assessments, patient-reported outcomes, and functional evaluations.

The safety observations support continued investigation of early postoperative use. No treatment-related infection, allergic reaction, wound dehiscence, maceration, or other postoperative wound complication was observed during the 16-week follow-up. Two participants developed transient postoperative erythema that was considered consistent with normal postoperative inflammatory responses rather than ON101 treatment and resolved spontaneously without sequelae. These observations indicate that application within three postoperative days was feasible and well tolerated in this cohort. Because the sample size was small, however, the study was not designed to establish comparative safety or detect uncommon complications.

Several limitations were found in this study. First, this was a small, single-center, nonrandomized controlled study, and selection bias and residual confounding cannot be excluded. Second, fracture patterns, fixation procedures, and incision locations were heterogeneous. Third, some participants contributed more than one evaluable incision site, introducing within-patient correlation that was not fully addressed by simple wound-level comparisons. Future studies should prespecify a patient-level index incision or use mixed-effects or generalized estimating-equation models. Fourth, follow-up was limited to 16 weeks, whereas linear scars may continue to evolve for many months. The present results therefore primarily reflect early scar maturation rather than final scar outcome. Finally, patient-reported pain, pruritus, tightness, satisfaction, scar-related quality of life, joint range of motion, and validated orthopedic functional outcomes were not assessed.

To our knowledge, this is the first prospective orthopedic study to evaluate ON101 during the early repair phase before complete epithelialization. Fulfilling the early prevention paradigm championed by the 2002 International Clinical Recommendations on Scar Management, early ON101 intervention optimizes the early repair phase and helps prevent scar worsening from the outset, rather than merely treating scars after they have formed. Future multicenter randomized trials should include larger cohorts, patient-level longitudinal analyses, longer follow-up, and direct functional and patient-reported assessments. Such studies will determine whether the early improvements in scar vascularity, pliability, height, color, and texture observed with ON101 translate into sustained improvements in scar quality, reduced pathological scar formation, preservation of joint function, and long-term orthopedic recovery.

Conclusion

Early postoperative administration of ON101, a topical wound care formulation, is associated with more favorable scar maturation after lower-extremity fracture fixation, as demonstrated by both total VSS score and standardized digital photography analysis. No major complications were found in this study,

supporting the safety and feasibility of this application. Larger randomized controlled trials are warranted to confirm these findings.

Abbreviations

GLCM
Gray-level co-occurrence matrix
SOC
Standard of care
VSS
Vancouver Scar Scale.

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (approval no. KSVGH22-CT11-16). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent to participate was obtained from all participants.

Consent for publication

Written informed consent for publication of the participants' clinical information and clinical photographs was obtained from all participants.

Competing interests

JCC is an employee of Oneness Biotech Co., Ltd., the developer and manufacturer of ON101. ON101 used in this study was supplied free of charge by Oneness Biotech Co., Ltd. JCC participated in study design and manuscript preparation. All clinical procedures, participant recruitment, blinded outcome assessments, and interpretation of the clinical findings were conducted independently by investigators at Kaohsiung Veterans General Hospital. SCL and KCL declare that they have no competing interests.

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Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because they contain potentially identifiable clinical and photographic information but are available from the corresponding author on reasonable request and subject to institutional and ethical approval.

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Figures

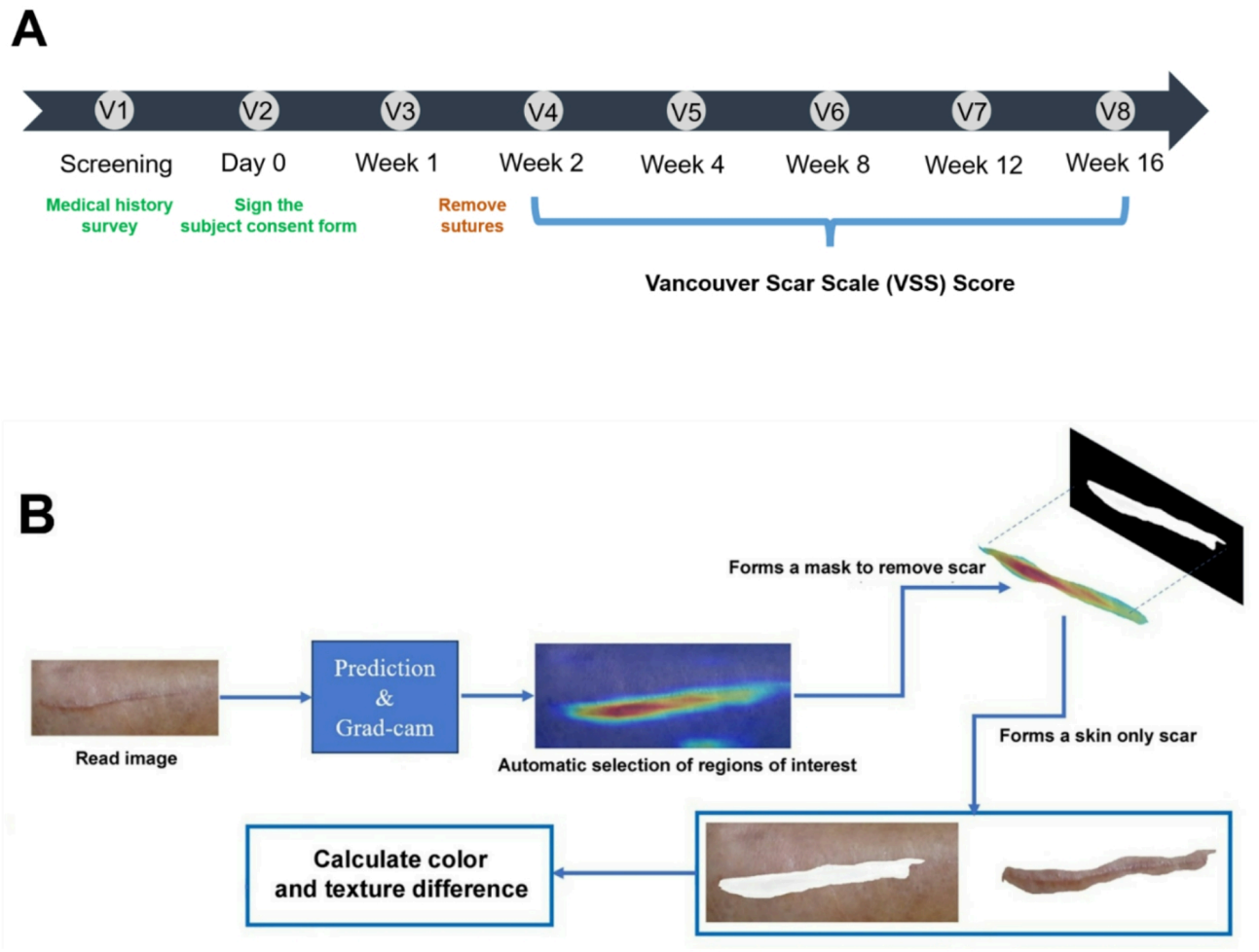


Figure 1

Workflow of clinical and digital scar assessments. (A) Clinical scar assessments and standardized photographs were obtained at each follow-up. (B) Photographs were segmented into scar and adjacent-skin regions. Color and texture features were quantified, and scar-to-skin difference ratios were calculated.

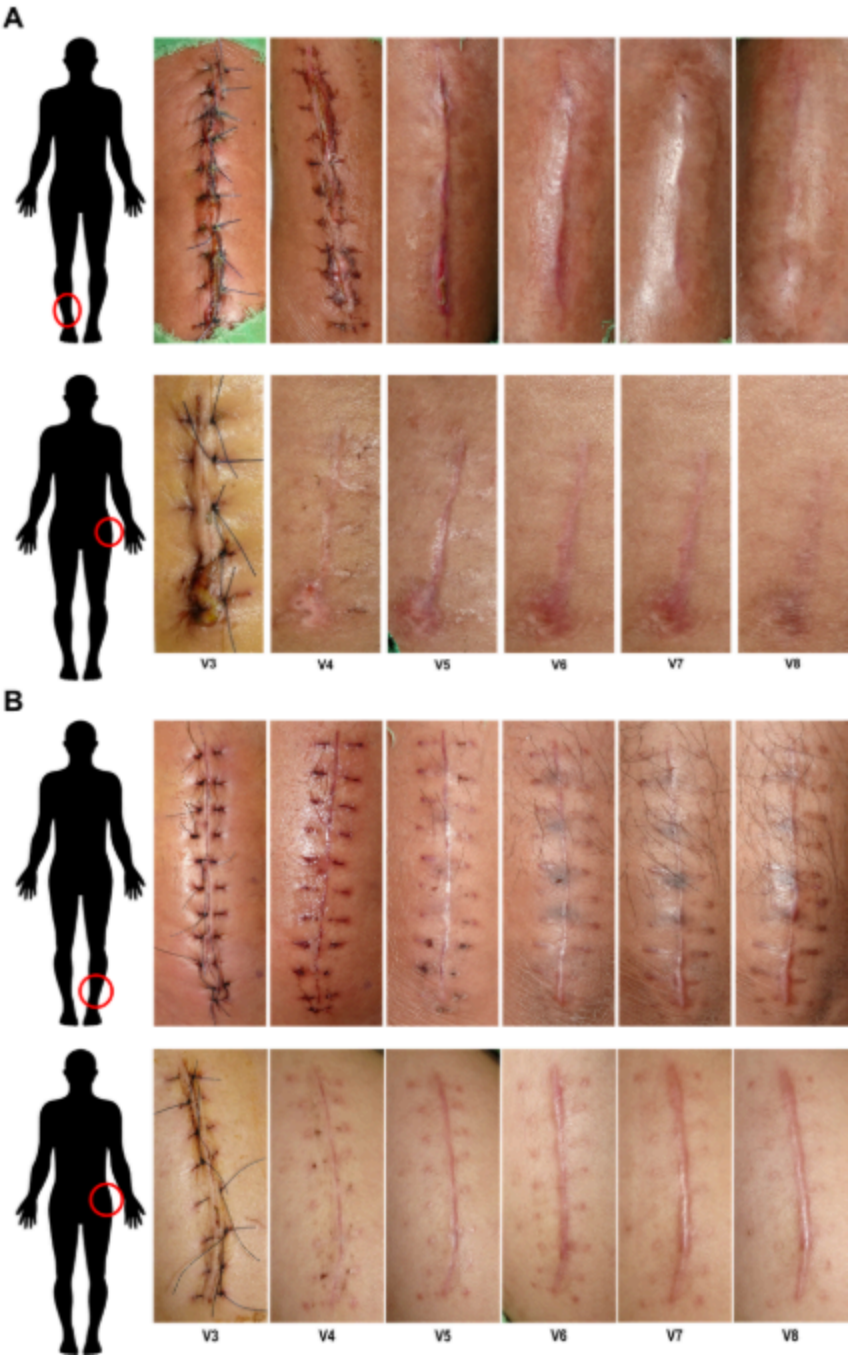


Figure 2

Representative serial photographs of matched orthopedic incision sites. (A) ON101 group: a 62-year-old woman with a sutured right-ankle wound (top) and a 32-year-old man with a sutured left-hip wound (bottom). (B) Control group: a 24-year-old man with a sutured left-ankle wound (top) and a 23-year-old man with a sutured left-hip wound (bottom). Images were obtained at Weeks 1, 2, 4, 8, 12, and 16 postoperatively.

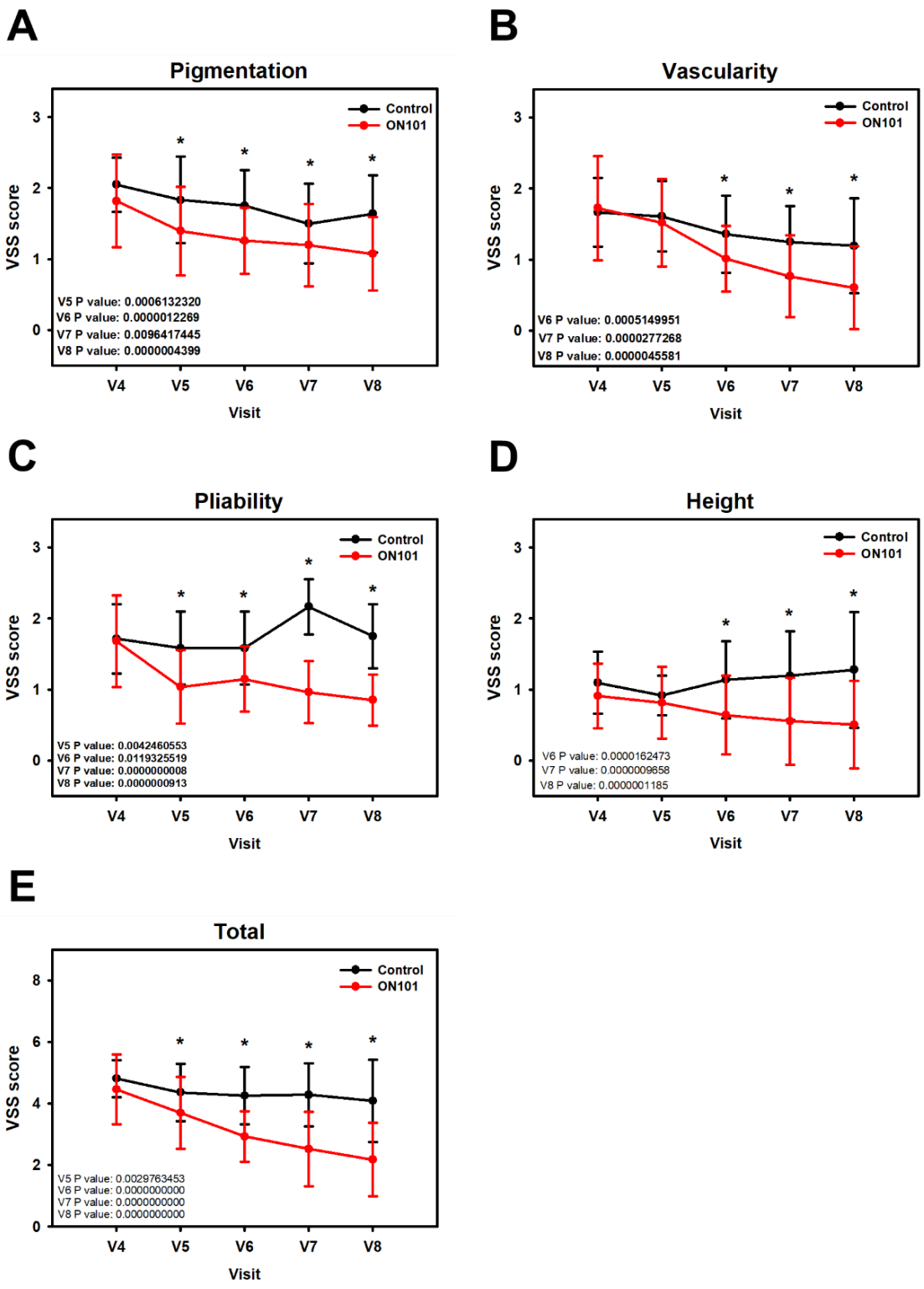


Figure 3

Longitudinal changes in Vancouver Scar Scale scores. Values are shown for total VSS score and the pigmentation, vascularity, pliability, and height domains from V4 (Week 2) to V8 (Week 16). Asterisks indicate statistically significant between-group differences at the corresponding time points.

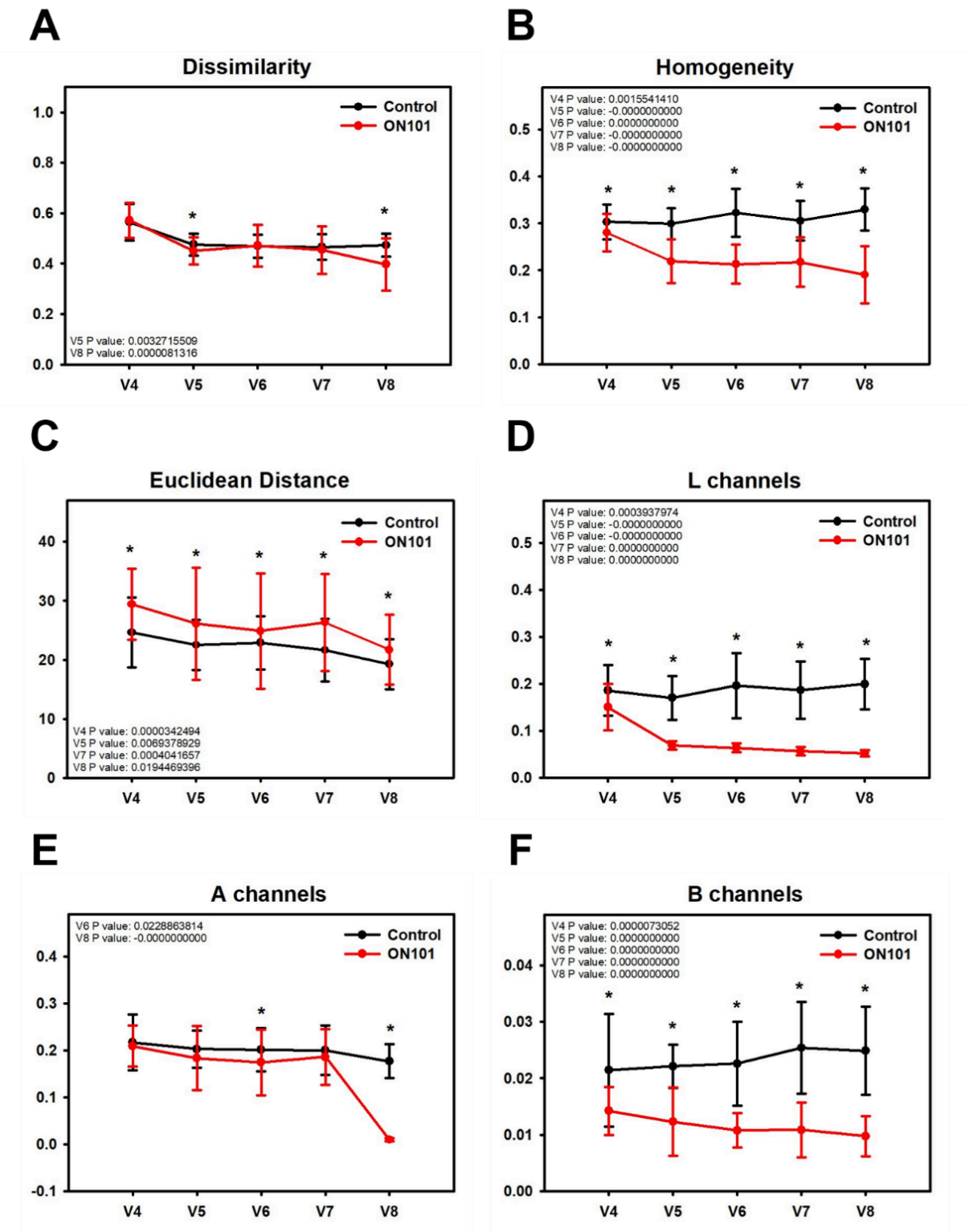


Figure 4

Longitudinal changes in digital scar texture and color. (A-B) Scar-to-skin difference ratios for GLCM-derived dissimilarity and homogeneity. (C) Euclidean distance in RGB color space. (D-F) Scar-to-skin difference ratios for the CIELab L*, a*, and b* components. Asterisks indicate statistically significant between-group differences at the corresponding time points.

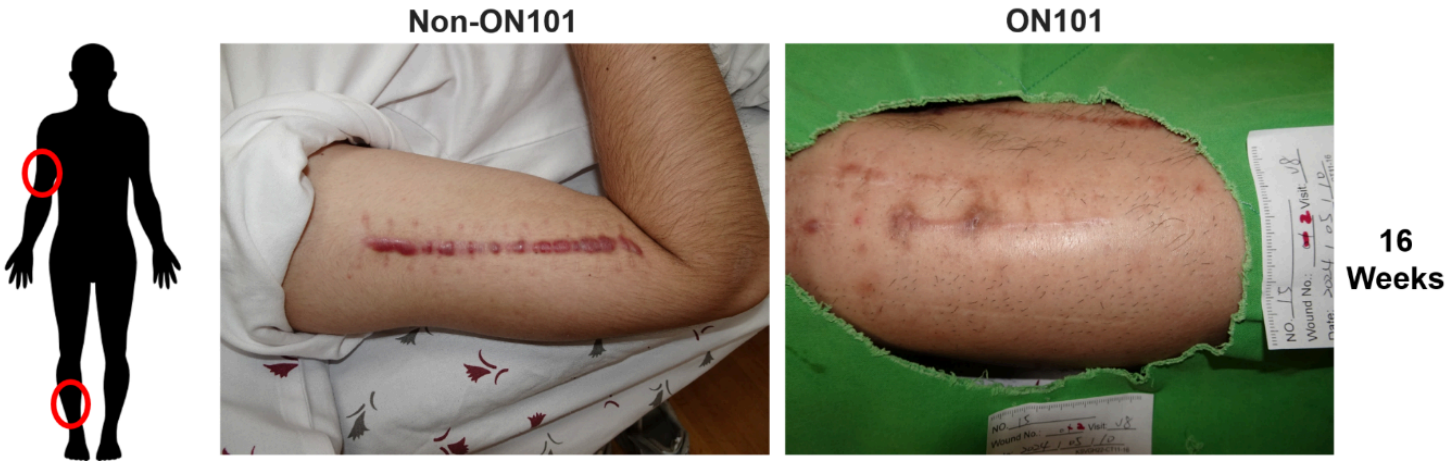


Figure 5

Within-participant comparison of two traumatic surgical wounds. A 21-year-old man had sutured wounds on the anterior right lower leg and right upper arm after a traffic accident. The lower-leg incision was treated with ON101 for 16 weeks, whereas the upper-arm wound received standard care. At Week 16, the ON101-treated lower-leg scar was less conspicuous, whereas the upper-arm scar remained visibly hypertrophic.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFig.1.docx