# Adipose Tissue-Derived Mesenchymal Stem Cell-Derived Exosomes Promote Wound Healing and Tissue Regeneration

Byong S. Cho<sup>1</sup>

<sup>1</sup>ExoCoBio Exosome Institute, Seoul, Korea, Rep. of South

# **Introduction & Objectives:**

Wound healing is a complex process involving cell proliferation, migration, and extracellular matrix (ECM) remodeling. Extracellular vesicles (EVs) or exosomes derived from adipose tissue-derived stem cells (ASCs) are emerging as promising alternatives to cell therapy for advanced wound healing. Hyaluronic acid (HA), a major component of the skin ECM, is widely utilized in wound dressings and dermal fillers. This study aimed to investigate the effects of ASC-derived exosomes (ASC-EXOs) on human dermal fibroblasts (HDFs) and their potential combination with HA in in vivo wound healing and dermal filler models. Furthermore, the combination of HA and ASC-EXOs may enhance wound healing and tissue remodeling, indicating its potential for both clinical and regenerative aesthetic applications in skin repair and regeneration.

#### Materials & Methods:

In vitro evaluation of ASC-EXOs was conducted in HDFs to assess their potential effects on cell proliferation, migration, and ECM remodeling. HDF proliferation assay revealed not only cell proliferation but also skin-related  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), fibroblast growth factor 2 (FGF2), and elastin expression levels. In a porcine wound healing model, topical treatment with a combination of HA and ASC-EXOs led to higher wound closure rates compared to HA alone. Histological analysis of re-epithelialization and collagen type III in wounds treated with the combination of HA and ASC-EXOs group and HA alone group. In a mouse dermal filler model, the combination of HA and ASC-EXOs or HA alone was subcutaneously injected into four dorsal sites of SKH1-hairless mice, and, after 3 weeks, the tissues surrounding the transplanted grafts were collected for histological analysis. Comparative analysis of the occurrence of vascularization and fibroblast infiltration, and the content of collagen III and collagen fiber in skin tissue between the HA and ASC-EXOs combination group and HA alone.

## Results:

The scratch-wound assay revealed that ASC-EXOs promoted the migration of HDFs into the cell-free area compared to the negative control. ASC-EXOs also induced the upregulation of mRNA expression levels of genes encoding collagen,  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), fibroblast growth factor 2 (FGF2).

In a porcine wound healing model, topical treatment with a combination of HA and ASC-EXOs led to higher wound closure rates compared to HA alone. Histological examination showed increased re-epithelialization and collagen type III deposition in wounds treated with the combination of HA and ASC-EXOs. In a mouse dermal filler model, tissues injected with the combination of HA and ASC-EXOs exhibited thicker tissue layers, increased vascularization, enhanced infiltration of myofibroblasts, and higher levels of collagen III and collagen fiber content compared to HA alone.

### **Conclusion:**

These results provide important insights into the potential therapeutic and cosmetic applications of ASC-EXOs in wound healing and tissue regeneration. Further studies are warranted to elucidate the underlying mechanisms of

ASC-EXO-mediated effects on wound healing and tissue regeneration, as well as to evaluate its safety and efficacy in clinical settings. Overall, the findings from this study suggest that ASC-EXOs, alone or in combination with HA, have the potential to be used as a novel therapeutic approach for wound healing and tissue regeneration in various clinical applications.

## Juvenile Gangrenous Vasculitis of the Scrotum: A Rare but Important Cause of Genital Ulceration

Ceren Nur Otlu\*<sup>1</sup>, gülhan aksoy saraç<sup>2</sup>, Selma emre evrensel<sup>3</sup>, Huban Sibel Orhun<sup>4</sup>

- <sup>1</sup>Ankara Bilkent Şehir Hastanesi, Dermatology and Venereology Clinic, Ankara, Türkiye
- <sup>2</sup>Ankara Bilkent Şehir Hastanesi, Dermatology and Venereology Clinic, Ankara, Türkiye
- <sup>3</sup>UFUK ÜNİVERSİTESİ DR. RIDVAN EGE HASTANESİ, Dermatology and Venereology Clinic, Ankara, Türkiye
- <sup>4</sup>Ankara Bilkent Şehir Hastanesi, Pathology Clinic, Ankara, Türkiye

# **Introduction & Objectives:**

The object of this case report were patient diagnosis is scrotal juvenile gangrenous vasculitis.

Scrotal juvenile gangrenous vasculitis is one of the rare causes of scrotal ulcers. It often occurs following an upper respiratory tract infection. It is characterized by an acute onset, sharply demarcated scrotal ulcers, typically fewer than five (often one) in number. It often occurs in young male patients. This disease heals with a scar. Recurrence is not seen. Due to its rarity, it is a clinical entity that may be overlooked or misdiagnosed; therefore, we emphasize increasing awareness.

Materials & Methods: In this case, we discuss a 17-year-old patient who presented with an ulcer on the scrotum. The patient had a one-week history of a lesion in the right scrotal area. On dermatological examination, there was an ulcer approximately 4x4 cm in size, with raised borders and a necrotic crust in the center. The patient had no known diseases or regular medication history. A week before the lesion appeared, the patient reported symptoms of fever and sore throat. There was no history of trauma, irritant topical substance use, or insect bites. When questioned for other signs of Behçet's disease, no additional findings were observed. Some blood tests and an ultrasound were requested from the patient. One punch biopsy and one direct immunofluorescence biopsy were taken from the lesion. Laboratory tests showed elevated CRP and ASO levels, but no other abnormal findings were noted. Tests for syphilis and herpes antibodies were negative. Scrotal USG was normal. The patient was treated with oral ampicillin-sulbactam and clindamycin for two weeks. For topical treatment betamethasone dipropionate and gentamicin combination were applied for three weeks. The ulcer healed within three weeks, leaving a scar. Histopathology revealed fibrin deposition and neutrophil clusters in the vessel walls. Direct immunofluorescence biopsy showed negativity for IgA, IgM, IgG, and positivity for C3C in the vessel wall.

**Results:** The histopathology result, along with clinical and laboratory findings, was evaluated as consistent with the diagnosis of scrotal juvenile gangrenous vasculitis.

**Conclusion:** The diagnosis of scrotal juvenile gangrenous vasculitis is still debated as to whether it is a separate clinical entity or a variant of pyoderma gangrenosum or the male variant of Lipschütz ulcers.

The Effect of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers on Reducing Pathologic Scar Formation After Median Sternotomy

Cansu Altınöz Güney\*<sup>1</sup>, Huriye Aybüke Koç<sup>2</sup>

<sup>1</sup>Dinar State Hospital, Department of Dermatology and Venereology, Afyonkarahisar, Türkiye <sup>2</sup>Prof. Dr. A. İlhan Özdemir State Hospital, Department of Dermatology and Venereology, Giresun, Türkiye

# **Introduction & Objectives:**

Pathological scars, like keloids, result from excessive dermal fibrosis and collagen deposition, causing discomfort, cosmetic issues, and restricted movement. Recent studies highlight the renin-angiotensin system's (RAS) role in tissue remodeling and wound healing. Angiotensin II (Ang II) drives fibrosis via AT1 receptors, promoting inflammation and angiogenesis, while AT2 receptors counteract fibrosis. Preclinical and animal studies support Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) for scar prevention, but human studies remain limited. This study aimed to investigate the effects of ACEIs and ARBs on pathological scar formation, following median sternotomy, focusing on the role of RAS in tissue remodeling and wound healing.

### Materials & Methods:

The observational study included 100 patients who had undergone median sternotomy at least 6 months prior and were receiving continuous antihypertensive treatment. Patients were categorized into three groups based on their medications: ACEIs (n=33), ARBs (n=35), and other antihypertensives (n=32). Scar formation was evaluated using the Patient and Observer Scar Assessment Scale (POSAS 2.0), which assesses both subjective and objective parameters. It consists of two numerical scales: PSAS evaluates pain, itching, color, stiffness, thickness, and irregularity, while OSAS covers vascularity, pigmentation, thickness, relief, pliability, and surface. Each parameter is rated 1–10, with total scores ranging from 6 (best) to 60 (worst).

## **Results:**

The demographic and clinical characteristics of the patients are summarized in Table 1. Keloid formation was significantly less common in the ACEI (24.2%) and ARB (25.7%) groups compared to the group using other antihypertensives (53.1%, p=.021). Both OSAS and PSAS total scores were significantly lower in the ACEI and ARB groups (p=.036 and p=.042, respectively). Among OSAS subparameters, vascularization (p=.005), pigmentation (p=.012), thickness (p=.010), and surface appearance (p=.007) were significantly improved in the ACEI and ARB groups. Among PSAS subparameters, pain (p=.003), stiffness (p=.021), thickness (p=.013), and irregularity (p=.025) were significantly lower in these groups compared to the other antihypertensives group.

## **Conclusion:**

ACEIs and ARBs, commonly used for hypertension, may help prevent keloid formation and improve scar outcomes. These medications offer a promising, cost-effective alternative to traditional scar treatments, particularly in hypertensive patients. Further human research is needed to fully explore their potential in scar management.

**Table 1.** The demographic and clinical characteristics of patients

Characteristics	Total (n=100)	ACEI (n=33 )	ARB (n=35)	Other (n=32)	P-value
Gender Male (%) Female (%)	76 (76%)	27 (81.8%)	24 (68.6%)	25 (78.1%)	.417
	24 (24%)	6 (18.2%)	11 (31.4%)	7 (21.9%)	
Age (mean±STD)	64.6±10.43	66.15±11.76	67.46±8.04	59.88±9.93	.005
Postoperative time, years	7.89±6.93	7.54±6.58	9.54±7.03	6.44±7	.084
Smoking (%)	9 (9%)	4 (12.1%)	3 (8.6%)	2 (6.2%)	.760
Alcohol (%)	12 (12%)	3 (9.1%)	6 (17.1%)	6 (18.7%)	.054
Keloid formation (%)	34 (34%)	8 (24.2%)	9 (25.7%)	17 (53.1%)	.021

p<0.05 was considered significant.

# Transplantation of autologous CFSE-labeled fibroblasts on gelatin microcarriers in a porcine wound-healing model

Shora Zamani Fekri\*<sup>1, 2</sup>, Rozalin Shamasha<sup>1, 3</sup>, Annika Starkenberg<sup>1</sup>, Jonathan Rakar<sup>1, 3</sup>, Gunnar Kratz<sup>1, 4</sup>, Johan PE Junker<sup>1, 3</sup>

# **Introduction & Objectives:**

Wounds are a worldwide problem in healthcare, incurring major costs annually. Extensive wounds require skin autotransplantation, which saves lives, but can result in donor-site morbidity, suboptimal outcomes, and are time-and resource-demanding. An alternative intervention, involving autologous cells seeded on microcarriers, may lead to improved outcome and can have advantages over cultured epithelial autografts. Understanding the contribution of cells and scaffolds to the healing process requires techniques for discriminating transplanted cells from resident cells. Using an intracellular fluorescent dye, carboxyfluorescein succinimidyl ester (CFSE), we tracked transplanted cells to analyze cell viability, proliferation, and tissue incorporation.

## **Materials & Methods:**

Autologous dermal fibroblasts were stained with CFSE, seeded on porous gelatin microcarriers (PGM), and transplanted to full-thickness porcine wounds on two female pigs, under approval from the regional animal ethics committee (ID 534). The experimental groups included wounds transplanted with PGM seeded with fibroblasts, PGM without cells, and non-transplanted control wounds. Wounded skin tissue was biopsied, cryosectioned, and analysed after three, seven, 14, and 28 days, post transplantation.

## **Results:**

CFSE-stained fibroblasts could be detected within the tissue at all timepoints. Transplanted fibroblasts had migrated out from the PGM and into the granulation tissue after three days. The fluorescence intensity of CFSE decreased over time, and was generally redistributed into the stroma as well as the epidermis. CFSE+ Ki67+ cells were detectable by immunohistochemistry and could be associated to tissue structures stained with pancytokeratin and alpha-SMA. After 14 days, the epidermal thickness of the wounds receiving empty PGM, and PGM + Fibroblasts, was significantly thicker compared to both the non-transplanted wounds and to uninjured skin. By day 28, the epidermis of all groups had matured, and no difference could be seen compared to uninjured epidermis.

## **Conclusion:**

The current study shows that CFSE is a stable marker for transplanted cells in tissue and can be followed in vivo for 28 days. These experiments confirm that transplanted fibroblasts seeded on PGM actively migrate out of the microcarriers and into the dermis. It was also evident that the fluorescence intensity of CFSE decreased over time, partly due to cell proliferation. Immunostaining for Ki67 indicates that some transplanted CFSE+ cells remain proliferative in the tissue. Future studies will focus on transplanting co-cultures of fibroblasts and keratinocytes

<sup>&</sup>lt;sup>1</sup>Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden

<sup>&</sup>lt;sup>2</sup>Department of Dermatology and Venereology, Linköping University Hospital, Linköping, Sweden

<sup>&</sup>lt;sup>3</sup>The Center for Disaster Medicine and Traumatology, Linköping University Hospital, Linköping, Sweden

<sup>&</sup>lt;sup>4</sup>Department of Hand Surgery, Plastic Surgery and Burns, Linköping University Hospital, Linköping, Sweden

and evaluating quality of healing after transplantation.

## Topical metformin in wound healing: a comprehensive systematic review of therapeutic outcomes

Dorian Maghsoodloo<sup>1</sup>, Hamed Zartab\*<sup>1</sup>, Abolfazl Parsi Mood<sup>1, 1</sup>, Alireza Firooz<sup>1, 1, 1, 1, 1</sup>

<sup>1</sup>Center for Research & Training in Skin Diseases & Leprosy, Tehran University of Medical Sciences, Tehran, Iran

# **Introduction & Objectives:**

Topical metformin has emerged as a promising candidate for accelerating wound repair through its multifaceted actions on angiogenesis, inflammation, autophagy, and antibacterial defense. This review critically examines preclinical and clinical investigations to elucidate its therapeutic potential in wound healing.

### **Materials & Methods:**

A systematic literature search across the PubMed, Scopus, Web of Science, Embase, and Cochrane databases, conducted until January 2025, identified 26 studies involving in vitro, in vivo, and clinical models.

#### **Results:**

These findings indicate that topical metformin enhances healing by increasing the expression of proangiogenic markers (VEGF, CD31, and  $\alpha$ -SMA), reducing the expression of proinflammatory cytokines, and promoting autophagy, especially when it is delivered via advanced biomaterial carriers such as hydrogels and nanofibers. Notably, only one study included clinical data.

### **Conclusion:**

Overall, topical metformin represents a novel therapeutic approach with significant potential to advance clinical wound care strategies. However, further human investigations are urgently needed to establish safe, effective, and optimal delivery methods.

## Construction of a Predictive Model for Post-Herpetic Skin Scars Based on LightGBM

Chuan Jiang<sup>1</sup>

<sup>1</sup>Bishan Hospital Affiliated to Chongqing Medical University (Chongqing Bishan District People's Hospital), Chongqing, China

## **Introduction & Objectives:**

To investigate the influencing factors of post-herpetic skin scars and to establish a predictive model using LightGBM.

### **Materials & Methods:**

A total of 215 patients diagnosed with herpes zoster who received treatment at our hospital were selected. Clinical data were collected, and patients were followed up for six months after the resolution of vesicles. Based on the occurrence of skin scars, patients were divided into a scar group and a control group. Univariate and multivariate logistic regression analyses were conducted to identify independent predictive factors for post-herpetic skin scars. Subsequently, a machine learning model using LightGBM was constructed.

## **Results:**

The incidence of post-herpetic skin scars in the 215 cases was 22.8% (49/215). Factors such as age (OR = 2.215, P = 0.046), diabetes mellitus (OR = 3.371, P = 0.048), lesion area (OR = 1.482, P = 0.012), and IgG level (OR = 0.158, P = 0.021) were identified as independent predictive factors for post-herpetic skin scars. The constructed model demonstrated an area under the curve (AUC) of 0.883 (95% CI: 0.781–0.957), with a sensitivity of 78.6%, specificity of 89.3%, and accuracy of 87.5%.

## **Conclusion:**

The machine learning model constructed using LightGBM shows promise in predicting post-herpetic skin scars.

### Cocaine-Levamisole-Induced Vasculitis Treated with IVIG and Secretions of Lucilia sericata

Zekayi Kutlubay<sup>1</sup>, Eylül Kasapoğlu\*<sup>1</sup>, Semih Bağhaki<sup>2</sup>, Tugba Kevser Uzuncakmak<sup>1</sup>, Ayşe Mine Önenerk Men<sup>3</sup>

<sup>1</sup>Cerrahpasa Medical Faculty Hospital, Department of Dermatology, Istanbul, Türkiye

**Introduction:** Cocaine is a widely used recreational drug, with up to 70% of seized cocaine containing levamisole, an additive known to cause cutaneous vasculitis characterized by necrosis and positive antineutrophil cytoplasmic antibodies (ANCAs). Histologically, it can result in a combination of leukocytoclastic vasculitis, thrombotic vasculitis, and/or vascular occlusion. We present a case of cocaine-induced vasculitis in a patient who had been smoking cocaine for over 20 years.

Case Presentation: A 58-year-old male with a history of long-term cocaine abuse presented to an external center with headache and fever. Initial iv antibiotic treatment for sinusitis was ineffective. Three days post-treatment, ulcerated lesions with erythematous bases appeared around the oral mucosa, spreading across the body (Figure 1). The lesions varied in depth, and there was significant necrosis and tissue loss around the mouth and jaw. His upper and lower lips and right soft palate were absent, the nasal septum was necrotic. Enterococcus faecalis was identified in wound cultures, and the diagnosis of gangrenous stomatitis was confirmed via biopsy. Despite hyperbaric oxygen therapy, iv antibiotics, and oral antifungals, the patient did not improve and was referred to our hospital.

Initial laboratory tests showed leukocytosis (WBC:  $13.5 \times 10^9$ /L), anemia (hemoglobin 10.3 g/dL), elevated erythrocyte sedimentation rate of 44 mm/h, and C-reactive protein level of 23.85 mg/L. Other metabolic, renal, hepatic, and immunological tests were within normal limits, and serological tests for various infections were negative. ANA panel was negative, but cANCA was positive.

4 mm punch biopsy and incisional biopsy from abdominal lesions were performed. Histopathology revealed ulcers in the epidermis, inflammatory cell infiltration in the dermis dominated by plasma cells, capillary vascular proliferation, and fibrosis (Figure 2). There was intimal thickening with thrombus formation in a medium-sized vessel in subcutaneous adipose tissue (Figure 3).

Rheumatology consultation suggested cocaine-associated vasculitis, considering the patient's long-term cocaine use. The biopsy results might have been affected by prior iv corticosteroid treatment. PET-CT scan, showed inflammatory changes in the skin and subcutaneous tissues. IVIG treatment was recommended. He received 2g/kg/month IVIG for five days and topical nadifloxacin with wet dressings and secretions of *L.sericata* were applied, resulting in decreased ESR and CRP values. After three weeks of hospitalization, the patient was discharged with instructions to continue IVIG treatment and wet dressings. Follow-up after three IVIG doses showed near-complete healing of trunk and facial lesions (Figure 4).

Thereafter, the patient was referred to the plastic surgery department for reconstructive surgery. He underwent bilateral perforator flap reconstruction. Both upper and lower lips were reconstructed at the same operation (Figure 5) and early postoperative follow up (3 months) was uneventful (Figure 6). The patient is scheduled for further minor aesthetic refinements six months postoperatively.

Conclusion: Cocaine-induced vasculitis should be considered in cocaine abusers presenting with painful rash and

<sup>&</sup>lt;sup>2</sup>Koç University Hospital, Department of Plastic, Reconstructive and Aesthetic Surgery, Istanbul, Türkiye

<sup>&</sup>lt;sup>3</sup>Cerrahpasa Medical Faculty Hospital, Department of Medical Pathology, Istanbul, Türkiye

skin necrosis. Given the rising use of cocaine, healthcare providers must maintain a high index of suspicion to diagnose and treat this condition effectively. Patient education on ceasing cocaine use is crucial.

Comparative efficacy of different types of Exosomes as Small extracellular vesicles (sEVs) in wound healing: A Network Meta-Analysis

Sami Salahia\*1

<sup>1</sup>Ain Shams University, Cairo, Egypt

# **Introduction & Objectives:**

Diabetic wounds pose a significant healthcare challenge due to delayed healing processes and increased risk of complications. Exosome-based therapies derived from various cellular sources have emerged as promising interventions. This study aims to evaluate the comparative efficacy of eleven exosome-based therapies in enhancing wound healing, with wound closure rate as the primary outcome.

### **Materials & Methods:**

A network meta-analysis was conducted to compare eleven exosome-based therapies: Placebo, Melatonin-stimulated human bone marrow mesenchymal stem cells-exosomes (MT hBMMSCExos), Menstrual blood-derived mesenchymal stem cells-exosomes (hMenSC-Exos), MicroRNA-126 Modified Mesenchymal Stem Cell-exosomes (miR-126-MSC-Exos), Nuclear factor erythroid 2-related factor 2 overexpressing adipose-derived stem cells-exosomes (Nrf2-ADSC-Exos or hADMSC-Nrf2-Exos), Fibrocyte-derived exosomes (Fibro-Exos), MicroRNA-126-overexpressing synovium mesenchymal stem cells-exosomes (SMSCs-126-Exos), Adipose-derived mesenchymal stem cell-exosomes (ADMSC-Exos or hADMSC-Exos), Human amniotic epithelial cell-exosomes (hAEC-Exos), Platelet-rich plasma-exosomes (PRP-Exos), and Human umbilical vein endothelial cell-exosome (HUVEC-Exo). Mean differences with 95% confidence intervals (CIs) were calculated to assess relative effectiveness

# **Results:**

Human umbilical vein endothelial cell-exosome (HUVEC-Exo) showed significant wound closure rates compared to Placebo with a mean difference of -43.25 (95% CI: -45.50, -41.00). Other therapies, such as Human umbilical cord blood-derived mesenchymal stem cell-exosomes (hUCB-MSC-Exos, -26.73; CI: -37.30, -16.16) and Plateletrich plasma-exosomes (PRP-Exos, -19.95; CI: -23.77, -16.13), demonstrated notable improvements. Adiposederived mesenchymal stem cell-exosomes (ADMSC-Exos, -9.89; CI: -13.24, -6.54) and Melatonin-stimulated human bone marrow mesenchymal stem cells-exosomes (MT-hBMMSC-Exos, -13.67; CI: -22.35, -4.99) also showed benefits over Placebo (-12.36; CI: -14.69, -10.03). Conversely, therapies like hMenSC-Exos (-1.31; CI: -10.29, 7.67) and Fibro-Exos (-2.75; CI: -12.51, 7.01) exhibited less pronounced effects.

## **Conclusion:**

Exosome-based therapies, particularly HUVEC-Exo, hUCB-MSC-Exos, and PRP-Exos, significantly enhance wound healing in diabetic wounds. These findings highlight their potential as innovative interventions for managing chronic wounds. Further clinical studies are warranted to validate these results and facilitate clinical translation.

# Mitochondria-Encoded Circ-mtRNR2 Enhances Diabetic Foot Ulcer Healing by Regulating Mitochondrial Dynamics in Fibroblasts

Jennifer Geara\*<sup>1</sup>, Guanglin Niu<sup>1</sup>, Yongjian Chen<sup>1</sup>, Yanwei Xiao<sup>2</sup>, Zhuang Liu<sup>1</sup>, Anna Wredenberg<sup>3</sup>, Pehr Sommar<sup>4</sup>, Aoxue Wang<sup>2</sup>, Ning Xu Landén<sup>1</sup>

<sup>1</sup>Karolinska Institute, Department of Medicine, Dermatology and Venereology Division, Solna, Sweden

**Introduction & Objectives:** Diabetic patients often experience impaired wound healing, most notable in the form of Diabetic Foot Ulcer (DFU), a chronic condition marked by non-healing ulcers accompanied by infection, neuropathy, and poor angiogenesis. Mitochondrial dysfunction, driven by excessive reactive oxygen species (ROS), plays a pivotal role in diabetes pathogenesis. However, a comprehensive understanding of the molecular mechanisms underlying DFU remains limited, hindering the development of effective treatments. Circular RNA (circRNA), known to regulate gene expression, hold therapeutic potential. RNA sequencing of donor-matched skin and day 7 wound-isolated cells identified differentially expressed circRNAs, including the mitochondria-encoded circular RNA Circ-mtRNR2, which was significantly downregulated in DFU, prompting investigation into its role in wound healing.

**Materials & Methods:** Circ-mtRNR2 stability and circularity were confirmed by RNAse R treatment, and its subcellular localization through fractionation. Its expression was evaluated under cytokine stimulation, hypoxia, and high glucose. Functional roles of Circ-mtRNR2 were studied via siRNA knockdown in Human Dermal adult Fibroblasts to assess cell proliferation, migration, and extracellular matrix (ECM) production. Mitochondrial function was analyzed by Seahorse assays, ROS levels via Mitosox staining and antioxidant gene expression by qRT-PCR. Mitochondrial dynamics (fusion and mitophagy) were also examined. Given that circRNA often exert their functions through protein interactions and to explore the molecular mechanisms underlying Circ-mtRNR2 activity, RNA pulldown followed by Mass Spectrometry was conducted, and binding was validated through RNA-binding protein immunoprecipitation (RIP) and Cellular Thermal Shift Assay (CETSA). The therapeutic potential of Circ-mtRNR2 was tested in human *ex vivo* and mouse *in vivo* wound models, evaluating tissue contraction and reepithelialization.

**Results:** Circ-mtRNR2 is mitochondria-localized and is induced by FGF2 but not by hypoxia or high glucose. It is significantly downregulated in DFU skin, particularly in the dermis. Functionally, Circ-mtRNR2 enhances fibroblast proliferation, migration, and ECM formation, while supporting mitochondrial respiration, reducing ROS, promoting antioxidant defenses, and regulating mitochondrial fusion and mitophagy. Mechanistically, Circ-mtRNR2 binds and stabilizes PRDX3, a mitochondrial antioxidant protein. This interaction, validated by RIP and CETSA, underscores the significance of Circ-mtRNR2 in maintaining redox balance. In both human and mouse wound models, Circ-mtRNR2 accelerated wound healing by promoting tissue contraction.

**Conclusion:** Circ-mtRNR2 promotes wound healing by enhancing fibroblast function and preserving mitochondrial homeostasis, thereby mitigating the toxic microenvironment associated with DFUs. These findings highlight the potential of Circ-mtRNR2 as a promising therapeutic target for tissue repair and DFU treatment. In turn, this deepens our understanding of DFU pathogenesis, paving the way for new drug targets, benefiting

<sup>&</sup>lt;sup>2</sup>The Second Hospital of Dalian Medical University, College of Integrative Medicine, Dalian Medical University, Department of Dermatology, Dalian, China

<sup>&</sup>lt;sup>3</sup>Karolinska Institute, Department of Medical Biochemistry and Biophysics, Solna, Sweden

<sup>&</sup>lt;sup>4</sup>Karolinska University Hospital, Department of Plastic and Reconstructive Surgery, Solna, Sweden

diabetic patients worldwide suffering from DFU or other hard-to-heal wounds.



## Understanding the microbiota in chronic leg ulcers with the use of shotgun metagenomics

Gabriela Gonzalez Matheus\*<sup>1, 2</sup>, Michelle Chamoun<sup>1</sup>, Yogeesan Sivakumaran<sup>3</sup>, Kiarash Khosrotehrani<sup>1, 2</sup>, Timothy Wells<sup>1</sup>

<sup>1</sup>The University of Queensland, Frazer Institute, Brisbane, Australia

**Introduction & Objectives:** Chronic wounds harbour a complex microbiome that can impact healing. To date, characterisation of the chronic wound microbiome profile largely relied on classical culture approaches and few studies have used next-generation sequencing platforms for high-resolution microbiome characterisation. We aimed to describe the microbiome profile of chronic wounds using metagenomic shortgun sequencing to investigate its role in wound healing.

Materials & Methods: A prospective cohort of patients with chronic lower limb ulcers was recruited from the Princess Alexandra and Logan Hospitals in Brisbane, Australia. Patient demographics and clinical data were gathered and categorized as diabetic/non diabetic, more or less than 12 months ulceration and finally through follow-up as healers and non-healers. A wound swab was taken at baseline from each participant and stored in RNAlater. Bacterial DNA extractions were carried out and submitted to metagenomic shotgun sequencing. Raw sequence reads were quality controlled using FastQC and taxonomic assignment was carried out with Kraken2. Data analyses were carried out using RStudio environment.

**Results:** A total of 45 participants were recruited. Principal component analysis separated the microbiotas of diabetic and non-diabetic ulcers (p=0.001) as well as ulcers of <12 and >12 months duration (p=0.007). Non-diabetic ulcers contained more *Pseudomonas* compared to diabetic ulcers (p=0.0002), and so were wounds >12 months duration (p=0.01). Non-healing wounds were significantly colonised by *Pseudomonas*, *Acinetobacter*, *Porphymonas* and *Campylobacter* genera, whereas healing wounds were associated with *Parviomonas* and *Trueperella*. Functional testing is currently underway.

**Conclusion:** Shotgun metagenomics confirmed that *Pseudomonas* was particularly abundant in non-diabetic ulcers and ulcers >12 months duration. The lower abundance of *Pseudomonas* in diabetic ulcers may reflect altered microbial dynamics due to the presence of other bacteria that thrive in a diabetic environment, such as *S. aureus*. In the context of longer-duration ulcers, the predominance of *Pseudomonas* might indicate a shift in microbial ecology, where less pathogenic species are replaced by more virulent or resilient organisms over time. Two genera of bacteria were associated with wound healing.

<sup>&</sup>lt;sup>2</sup>Princess Alexandra Hospital, Dermatology, Brisbane, Australia

<sup>&</sup>lt;sup>3</sup>Princess Alexandra Hospital, Vascular Surgery, Brisbane, Australia

# Post-Transcriptional Dynamics of Fibroblasts and KeratinocytesDuring Skin Wound Healing

Lihua Luo<sup>1</sup>, Zhuang Liu<sup>1</sup>, Ningxu Landén<sup>1</sup>

<sup>1</sup>Karolinska Institutet, Stockholms, Sweden

**Introduction & Objectives:** Skin wound healing involves coordinated actions of fibroblasts (FB) and keratinocytes (KC), yet their transcriptomic regulation—especially at the isoform and post-transcriptional levels—remains poorly understood. Short-read sequencing limits the resolution of full-length transcripts and isoform diversity.

This study aims to define the dynamic transcriptomic profiles of FB and KC during wound healing using a multiomics approach, focusing on isoform identification, splicing, promoter usage, polyadenylation, and microRNA interactions to uncover key regulatory mechanisms in tissue repair.

**Materials & Methods:** A comprehensive multi-omics strategy was employed to investigate transcriptomic regulation in fibroblasts (FB) and keratinocytes (KC) from intact and wounded skin. Full-length transcriptomes were generated by integrating long-read PacBio Iso-Seq with short-read RNA-seq. Bulk RNA-seq was used to quantify gene expression, assess intron retention, and evaluate alternative promoter usage. Smart-seq2 single-cell RNA-seq enabled the resolution of cell-type-specific exon-skipping events. Single-cell 3' RNA-seq provided dynamic profiling of alternative polyadenylation (APA) across wound healing stages. Additionally, small-RNA sequencing was used to analyze microRNA expression and its interaction with APA events. Together, these multi-layered omics datasets enabled high-resolution analysis of transcriptional and post-transcriptional regulatory mechanisms during skin repair.

**Results:** We identified 7,564 and 6,728 non-redundant full-length transcripts in fibroblasts (FB) and keratinocytes (KC), respectively, with 12.5% and 11.1% representing novel isoforms. Additionally, seven types of alternative splicing events showed dynamic regulation during wound healing. Both major and minor promoters contributed to the fine-tuning of gene expression, while exon-skipping patterns were cell-type-specific, indicating distinct regulatory programs. Furthermore, APA analysis revealed increased usage of proximal polyadenylation sites in proliferating and migrating cells on day 7, which declined by day 30. As a result, transcript shortening reduced microRNA binding potential, suggesting a mechanism by which transcripts may evade microRNA-mediated repression during tissue repair.

**Conclusion:** This multi-omics study reveals novel post-transcriptional mechanisms regulating gene expression in fibroblasts and keratinocytes during wound healing. By integrating long- and short-read sequencing, we provide a high-resolution transcriptomic resource that advances understanding of tissue repair and highlights potential therapeutic targets.

## The Contribution of Complementary Examinations in the Etiological Assessment of Chronic Leg Ulcers

LEILA BENAHMED<sup>1</sup>, Ouissal Hormi<sup>1</sup>, Nada Tahri<sup>1</sup>, Nassiba Zerrouki<sup>1, 2</sup>, Nada Zizi<sup>1, 2</sup>

<sup>1</sup>Mohammed VI University Hospital Center, Oujda, Dermatology, Venereology, and Allergology Department, Mohammed VI University Hospital Center, Oujda, Oujda, Morocco

<sup>2</sup>Faculty of Medicine and Pharmacy of Oujda, Epidemiology, Clinical Research, and Public Health Laboratory, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco, Oujda, Morocco

**Introduction & Objectives:** Chronic leg ulcers represent a major diagnostic and therapeutic challenge, involving complex etiology, delayed healing, and functional and psychosocial complications. They often signal underlying diseases requiring personalized management. Although clinical examination is vital for initial diagnosis, it must be supplemented by specific tests to identify the underlying causes and guide therapeutic strategies. This study evaluates the role of complementary examinations in the etiological diagnosis of chronic leg ulcers.

**Materials & Methods:** This retrospective study, conducted in the dermatology department of a university hospital over an 11-year period, included patients hospitalized for chronic leg ulcers. Collected data included demographics, complementary tests, and their contribution to etiological diagnosis. Biological, vascular, and histopathological examinations were performed according to standard protocols.

**Results:** The study included 31 patients with a mean age of  $48 \pm 22$  years, comprising 17 men and 14 women, yielding a sex ratio of 1.21 M/F.

Biological tests were performed in 90.3% of patients, revealing abnormalities in inflammatory markers in 64.5% of cases, immunological abnormalities in 12.9%, and disturbances in phosphorus-calcium balance in 3.2%.

Microbiological sampling was conducted in 48.4% of patients, yielding positive results in 32.3% of cases, including infectious ulcers and superinfected ulcers.

Skin biopsy, performed in 83.9% of patients, confirmed the etiological diagnosis in 61.3% of cases, particularly aiding in the diagnosis of tumor-related and inflammatory ulcers.

Vascular assessment using Doppler ultrasound and/or CT angiography was performed in 51.6% of patients, revealing vascular impairment in 39.2% of cases. Computed tomography angiography (CTAP) was conducted in 51.6% of patients to assess the extent of tumor, infectious, and systemic lesions.

A karyotype was performed in 3.2% of patients, identifying two additional chromosomal markers of unknown origin, necessitating further molecular cytogenetic analysis.

In terms of diagnosed etiologies, vascular ulcers accounted for 35.5% of cases, including 25.8% venous ulcers and 3.2% arterial ulcers. Tumor-related ulcers were identified in 6.4% of cases, including squamous cell carcinoma and cutaneous T-cell lymphoma. Infectious ulcers represented 16.1%, including bacterial (tuberculosis), parasitic (leishmaniasis), and fungal (eumycetoma) origins. Neuropathic ulcers were diagnosed in 3.2% of patients, while post-burn ulcers were observed in 9.6% of cases. A pressure ulcer was noted in a bedridden patient with a history of spina bifida. Additionally, multiple ulcers were observed in a young patient with chromosomal abnormalities, though the final syndromic diagnosis remains undetermined.

**Conclusion:** Complementary examinations are essential for diagnosing chronic leg ulcers. Their rational use improves the identification of ulcer etiology and helps tailor appropriate treatment. A structured diagnostic

algorithm, based on clinical signs, could enhance investigation efficiency, optimize management, and reduce delays. Multidisciplinary collaboration among specialists is key for providing optimal care to these patients.

# "Dual Injectable and Topical Platelet-Rich Fibrin Therapy for Post-Burn Keloids: A Case Report"

Fatima Shamim\*<sup>1</sup>, Ketevan Berianidze<sup>2</sup>

<sup>1</sup>Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia

**Introduction & Objectives:** Keloid formation after burns remains a significant therapeutic challenge due to excessive myofibroblastic activity and frequent recurrence. Traditional treatments including corticosteroids, silicone sheets, and surgical excision show only modest long-term success. Recent literature highlights promising results with PRP and PRF as regenerative approaches, attributed to their high concentration of growth factors that promote tissue remodeling and regulate fibroblast function. We present a case of a 25-year-old female with a symptomatic deep keloid formed below the umbilicus following a hot water burn, treated with a novel approach combining injectable and topical PRF therapy.

**Materials & Methods:** The patient was managed with four PRF treatment sessions in 2-week intervals. Plateletrich fibrin (PRF) is a second-generation autologous blood concentration that creates a fibrin matrix and includes platelets, leukocytes, and cytokines. Unlike PRP, PRF doesn't contain anticoagulants and gelling agents so when implanted, it allows slow and continuous release of growth factors with reduces inflammation and edema, promoting faster and better healing and tissue regeneration.\*\* Its unique gel consistency permits both injection and topical application. In our case, PRF was administered sub-lesionally during each session. Additionally, remaining PRF was applied topically on sterile gauze directly over the scar to maintain asepsis, while a custom formulation containing 2.5 mg PRF in 14 g neutral cream base was applied every 2-3 days. Epicin cream provided complementary antimicrobial support. All PRF preparations were refrigerated and utilized within hours. Vancouver Scar Scale (VSS) parameters—vascularity, pigmentation, pliability and height—assessed keloid severity before and after treatment.

**Results:** Following four PRF sessions, we observed remarkable improvement in VSS score from 10 to 4, with specific improvements in vascularity  $(3\rightarrow1)$ , pigmentation  $(2\rightarrow1)$ , pliability  $(3\rightarrow2)$ , and height  $(2\rightarrow0)$ . The patient reported significant reduction in pain and pruritus. Notably, the keloid decreased from an elevated 2-5mm to skin level. No adverse effects occurred, and at 3-month follow-up, no recurrence was detected, though longer monitoring continues as keloids may recur months or years after treatment. This dual-application PRF approach appeared to work synergistically, providing deeper tissue remodeling through direct growth factor delivery while supporting surface epidermal renewal.

**Conclusion:** This case shows a PRF's potential for being a safe and effective treatment adjunct for post-burn keloid scarring. Dual application (injectable and topical) was in order to increase its regenerative potential as growth factors will be released slowly at the site of treatment and might modulate the activity of fibroblasts and collagen deposit. It is autologous and minimally invasive and offers the relative advantages over conventional treatments. PRF therapy is a promising treatment for patients with recurrent keloids that are otherwise resistant to treatment and needs further exploration in larger controlled trials with long-term follow-up before long-term effectiveness and recurrence can be tentatively concluded.

<sup>&</sup>lt;sup>2</sup>Caucasus University, Department of Dermatology, T'bilisi, Georgia

## Diagnostic Confusion: Multiple Vascular Leg Ulcers Mimicking Kyrle's Disease: A Case Report

wissal souhail<sup>1, 2</sup>, Layla Bendaoud<sup>1, 2</sup>, Meryam Aboudourib<sup>1, 2</sup>, Ouafa Hocar<sup>1, 2</sup>, Said Amal<sup>1, 2</sup>

<sup>1</sup>CHU Mohammed VI, Arrazi hospital, dermatology department, MARRAKECH

# **Introduction:**

Leg ulcers are a chronic pathology, often of vascular origin, with slow healing and frequent complications. Their clinical presentation can be atypical, especially in diabetic patients, making differential diagnosis sometimes challenging. Among the rare diagnoses to consider is Kyrle's disease, an acquired perforating dermatosis that can complicate the progression of diabetes mellitus.

### **Observation:**

A 64-year-old patient with poorly controlled insulin-resistant diabetes for 10 years, under insulin therapy, presented 8 months ago with pruritic, papulovesicular, hyperkeratotic lesions, featuring a central corneal plug and recurrent ulcerations on the lower limbs. The patient also had a motor walking disturbance with steppage. Infectious work-up and generalized pruritus were normal, but an elevated HbA1c and disturbed glycemic cycle were noted. Skin biopsy did not confirm Kyrle's disease, but bacterial culture revealed Serratia marcescens, and mycology was negative. Vascular exploration revealed diffuse atherosclerotic overload with stenosis and occlusion of the tibial arteries. Electromyography (EMG) showed diabetic neuropathy. The treatment included vascular protection (acetylsalicylic acid, statin, ramipril), angioplasty, and management of neuropathic pain with pregabalin. A directed local treatment for ulcer healing, keratolytic therapy for hyperkeratosis, and LED therapy resulted in significant improvement after 4 weeks, with reduced ulcer size and pain.

# discussion:

Kyrle's disease presents a characteristic clinical picture, including pruritic, papulovesicular, and hyperkeratotic eruptions, often seen in diabetic patients. It can be confused with conditions such as nodular prurigo, hypertrophic lichen planus, Flegel's disease, or arterial leg ulcers. The latter, often non-exudative, can form a thick corneal layer, promoting impaired reepithelialization, which resembles our patient's condition. Kyrle's disease is commonly associated with diabetes mellitus (50%) and end-stage chronic renal failure (70%), often in the context of longstanding diabetes. Although its pathophysiology remains poorly understood, factors such as skin trauma and diabetic vasculopathy contribute to this clinical similarity. Motor neuropathy in diabetics can lead to lesions from friction forces and hyperkeratotic calluses, while anhidrosis can cause dry skin, leading to hyperkeratosis, as observed in our patient.

Leg ulcers typically take an average of six months to heal, explaining the frequent complications such as infections or intolerance to local treatments. A biopsy is necessary to exclude atypical conditions, such as carcinoma. The use of LED therapy for leg ulcers, combined with appropriate local treatment, has shown enhanced efficacy, promoting healing and reducing pain and infection.

### Conclusion:

The similarity between Kyrle's disease and arterial leg ulcers in elderly diabetic patients poses a diagnostic challenge. Our patient's case highlights the importance of a rigorous diagnostic and therapeutic approach,

<sup>&</sup>lt;sup>2</sup>Biosciences Research Laboratory, FMPM, Cadi Ayyad university, MARRAKECH

especially in the early stages, to avoid unnecessary diagnostic pitfalls and ensure effective management.

# TGF-β signaling-mediated wound healing is required for hair follicle neogenesis

Tatsuya Ogawa<sup>1, 2</sup>, Chae Ho Lim<sup>1</sup>, Hideyuki Kosumi<sup>1</sup>, Olivia Yeroushalmi<sup>1</sup>, Priya Marella<sup>1</sup>, Raaita Anwar<sup>1</sup>, Annette Kaminaka<sup>1</sup>, Soung Hoon Lee<sup>1</sup>, Mayumi Ito<sup>1</sup>

<sup>1</sup>NYU Grossman School of Medicine, The Ronald O. Perelman Department of Dermatology, New York, United States

<sup>2</sup>University of Tsukuba, Department of Dermatology, Tsukuba, Japan

# **Introduction & Objectives:**

Mammalian adult skin wounds typically end in fibrosis and fail to regenerate skin appendages, such as hair follicles (HFs). Our previous studies demonstrated that new HFs regenerate in the center of large full-thickness wounds of mice following wound healing. However, it remains unclear how the initial wound healing mechanisms are linked to the later HF neogenesis (HFN). Transforming growth factor- $\beta$  (TGF- $\beta$ ) is a pivotal mediator in wound healing, promoting myofibroblast differentiation and extracellular matrix deposition, including collagen, in the wound dermis. We aimed to understand HFN-competent tissue state, specifically focusing on TGF- $\beta$  signaling-mediated wound healing.

## **Materials & Methods:**

Multiple genetically modified mouse models were used to deplete TGF- $\beta$  signaling or its downstream targets. 3-to-8-week-old mice were subjected to large excisional wounding and evaluated for their ability to induce HFN.

## **Results:**

Conditional knockout of TGF- $\beta$  receptor 2 in wound fibroblasts before but not after re-epithelialization inhibited HFN and reduced myofibroblast differentiation and collagen deposition. These results suggest that TGF- $\beta$  signaling during wound healing is critical for HFN. Further, conditional knockout of collagen type I in wound fibroblasts also inhibited HFN, which was rescued by the activation of the Sonic hedgehog (Shh) signaling. Spatial transcriptomic analysis further revealed that the absence of TGF- $\beta$  signaling disrupted macrophage infiltration and chemoattractant expression, major players in wound healing and HFN, as well as Shh signaling activation in the wound dermis.

# **Conclusion:**

Collectively, our results suggest that TGF- $\beta$  signaling orchestrates wound healing process by sufficient collagen deposition and macrophage recruitment in the wound dermis, which may provide the regenerative microenvironment to initiate HFN.

## A Rare Case of Facial Pyoderma Gangrenosum Triggered by Needle Electrolysis

Nazmiye Selin Salici\*<sup>1</sup>, gunel rasulova<sup>1</sup>, Defne Ozkoca<sup>1</sup>, Nesimi Buyukbabani<sup>2</sup>, Sumeyre Seda Ertekin<sup>1</sup>

<sup>1</sup>Koc University School of Medicine, Department of Dermatology and Venereology, Istanbul, Türkiye <sup>2</sup>Koc University School of Medicine, Department of Pathology, Istanbul, Türkiye

# **Introduction & Objectives:**

Pyoderma gangrenosum (PG) is a rare and painful neutrophilic dermatosis that typically presents as a rapidly progressive ulcer with undermined, violaceous borders. Although its exact pathogenesis remains unclear, PG is often associated with systemic conditions, and pathergy is recognized as a major triggering factor. The disease most commonly affects the lower extremities and trunk, while head and neck involvement is rare, accounting for less than 8% of reported cases. Herein, we present a rare case of facial PG following needle electrolysis in a young woman with a personal and family history of autoimmune diseases, including Hashimoto's thyroiditis and alopecia areata.

### Case Presentation:

A 25-year-old woman presented with a three-day history of a painful, solitary ulcer on the left preauricular region. Twenty days earlier, she had undergone needle electrolysis for permanent hair removal on both sideburn areas at an external center. Shortly after the procedure, severe inflammatory reaction developed at the treated sites, evolving into erosions. She was initially managed with topical antibiotics and epithelializing agents. While both lesions progressed to crusting, the lesion on the left side rapidly ulcerated within the last three days. Her medical history included Hashimoto's thyroiditis and alopecia areata capitis, resistant to topical, intralesional, and systemic corticosteroid treatments since 2022. She also had a family history of alopecia universalis in her brother. There were no symptoms of connective tissue disease or inflammatory bowel disease. Dermatological examination revealed a violaceous, undermined, full-thickness ulcer with irregular borders on the left preauricular area. Histopathological examination of a punch biopsy from the ulcer margin demonstrated an inflammatory infiltrate composed of neutrophils and mononuclear in dermis and subcutaneous tissue, accompanied by neovascularization and focal areas of myxoid change. Fungal and bacterial cultures were negative. Based on the clinical history, lesion characteristics, a positive pathergy response, and histological findings, a diagnosis of pyoderma gangrenosum was established. Autoantibody screening for autoimmune connective tissue and inflammatory bowel diseases was negative. Systemic corticosteroid therapy with with prednisone (0.5 mg/kg/day) was initiated, leading to a rapid and marked clinical improvement.

## **Conclusion:**

Over half of PG cases are associated with autoimmune or systemic diseases, most frequently inflammatory bowel disease, arthritis, and hematologic disorders. The co-occurrence of alopecia areata and Hashimoto's thyroiditis in this case supports the link between PG and immune dysregulation. Moreover, facial involvement represents an uncommon localization of PG, accounting for less than 8% of cases, which adds to the diagnostic challenge. In the literature, systemic immunosuppressive therapies such as corticosteroids or cyclosporine are commonly initiated in cases of facial PG due to the high risk of functional and cosmetic sequelae. Given the high disease burden associated with lesions in cosmetically sensitive areas, early recognition and timely intervention in facial PG are essential to minimize scarring and optimize patient outcome.

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A critical review and update of Buruli Ulcer in Australia – what Dermatologists need to consider when assessing ulcers.

Andjela Arandjelovic\*1

<sup>1</sup>James Cook University, Townsville, Australia

**Objective:** To evaluate current epidemiological trends, transmission pathways, and effective prevention strategies for Buruli Ulcer in Australia, and to determine key differentiating features when assessing a patient with an ulcer.

**Background:** The rising incidence and geographic spread of Buruli Ulcer in southeastern Australia, particularly in temperate coastal Victoria, highlights the importance of understanding it's epidemiological patterns, unique clinical features, modes of transmission and feasible prevention strategies.

**Methods:** A narrative review was conducted using EMBASE and PubMed databases. Search terms included "Buruli Ulcer" OR "*Mycobacterium ulcerans*" AND "epidemiology" OR "clinical features" OR "transmission" OR "prevention" AND "Australia". The search was limited to English-language publications from January 2015 to April 2025, including peer-reviewed articles, books and government public health reports. Studies unrelated to Australia or published in non-English languages were excluded.

**Results:**\* This review synthesised findings from epidemiological studies, environmental microbiology and public health research to outline the current understanding of Buruli Ulcer in Australia. A total of fifteen publications were included in this review.\*

**Discussion:**\* In Australia, Buruli Ulcer exhibits distinct epidemiological patterns, with marked concentration in coastal areas including the Bellarine and Mornington Peninsulas. Evidence suggests transmission may occur through environmental exposure (e.g. contaminated soil or water), vector-borne pathways (notably via mosquitoes), and zoonotic reservoirs (possums). Patients with epidemiological risk factors and a non-healing, progressive ulcer warrant further investigation. Early clinical features include a painless, erythematous nodule; however, these eventually erupt into ulcers with undermined edges, surrounding induration and a necrotic base. PCR testing through a swab or skin biopsy are required for diagnosis. Prevention strategies should also focus on education, mosquito bite prevention, reduction in mosquito and possum burden and environmental management.

**Conclusion:**\* The ongoing rise in Buruli Ulcer in Australia warrants improved understanding in the epidemiology, transmission and clinical features of this disease. Early detection is associated with reduced severity of cutaneous lesions and more effective management. Targeted prevention strategies informed by current evidence are essential to mitigate the spread of this debilitating and emerging public health threat.

Epidermal regeneration in recessive dystrophic epidermolysis bullosa following treatment with birch bark extract: insights from line field confocal optical coherence tomography imaging

Maria Rita Nasca\*<sup>1</sup>, Anna Elisa Verzi<sup>1</sup>, Giuseppe Micali<sup>1</sup>, Francesco Lacarrubba<sup>1</sup>

<sup>1</sup>Dermatology Clinic, University of Catania, Catania, Italy

# **Introduction & Objectives:**

Topical birch bark extract (Oleogel-S10) has recently been approved both in Europe and in the UK for the topical treatment of partial-thickness wounds in patients with recessive dystrophic epidermolysis bullosa (RDEB). Line-field confocal optical coherence tomography (LC-OCT) is a novel non-invasive laser-based technique that has demonstrated to be useful in the diagnosis and monitoring of several skin disorders, thanks to its ability to provide in vivo real-time skin imaging. In this study the potential of LC-OCT for in vivo monitoring of wound healing in RDEB has been explored.

### **Materials & Methods:**

Four patients with RDEB (3 males, 1 female; mean age 48.5 years, range 36–61) applied topical birch bark extract (Oleogel-S10) once daily over a 6-week period. In each patient, two target wounds for a total of eight lesions were selected for close monitoring. Healing of selected lesions was assessed at baseline, weekly, and at study completion using both standard photography and LC-OCT imaging. The reduction in wound surface area, duration of wound closure, time to wound closure, and subjective symptoms (pain and itching) as well as LC-OCT aspects were recorded at each time point.

## **Results:**

By week 2, all patients showed clinical improvement, with LC-OCT detecting early signs of re-epithelialization. After 6 weeks, complete clinical healing of the target wounds was observed in all cases with no reported adverse effects, along with marked reductions in pruritus and pain and complete re-epithelialization at LC-OCT.

# **Conclusion:**

LC-OCT imaging confirmed early full epidermal regeneration, including a fully developed stratum corneum, in patients with RDEB following the topical application of birch bark extract as soon as after a few days. In addition, it allowed a timely non-invasive temporal evaluation of changes during progressive wound re-epithelialization. This in vivo model demonstrated that LC-OCT enables non-invasive, real-time tracking of wound healing dynamics in RDEB, supporting its potential for broader application in non-invasive dermatological research.

# Biological Effects of Capacitive-Resistive Electric Transfer Therapy on Human Keratinocytes and Fibroblasts: Implications for Wound Healing

Elena Toledano-Macías<sup>1</sup>, María Luisa Hernández-Bule<sup>1</sup>, María Antonia Martínez-Pascual<sup>1</sup>, Jorge Naharro-Rodriguez<sup>2</sup>, Emilio García-Mouronte<sup>2</sup>, Luis Alonso<sup>2</sup>, Montserrat Fernandez-Guarino<sup>2</sup>, Luis Alfonso Pérez-González\*<sup>2</sup>

<sup>1</sup>Laboratorio de Fotobiología y Bioelectromagnetismo., Madrid

**Introduction & Objectives:** Clinical practice has shown that non-invasive capacitive-resistive electric transfer (CRET) therapy may improve healing in patients with slow-to-heal wounds. Wound healing is a complex process involving various cellular mechanisms such as inflammation, proliferation, and cell migration. These processes may potentially be modulated by CRET therapy, based on current scientific evidence.

To investigate the effects of CRET on proliferation, inflammation, and migration in human keratinocytes (HaCaT) and fibroblasts (HF) using an in vitro model simulating real wound closure.

**Materials & Methods:** HaCaT and HF cultures were treated under subthermal conditions for 5 minutes every 4 hours using the following parameters and equipment:  $100 \,\mu\text{A/mm}^2$ ;  $448 \,\text{kHz}$ ; Device: ELITE NS, INDIBA S.A, over a 48-hour period. Control cultures of both cell types were maintained under identical conditions but were not exposed to radiofrequency. Proliferation was assessed using the XTT assay; wound closure was evaluated through wound assay (WA); and immunofluorescence was used to assess adhesion and migration proteins (β-catenin, E-cadherin, and vimentin). In HaCaT cells, ELISA was conducted to quantify cytokines: IL-8, MIP-1, MCP-1, and RANTES.

**Results:** The CRET-treated group exhibited a statistically significant increase in proliferation in both cell types compared to controls. Additionally, CRET reduced membrane expression of  $\beta$ -catenin and E-cadherin, while increasing vimentin expression. The WA assay revealed accelerated migration in HF, while HaCaT migration was slower than in controls. Furthermore, CRET therapy increased MCP-1 expression by 19%, while IL-8 and RANTES levels were reduced. No significant differences were found in MIP-1 expression between groups.

**Conclusion:** CRET enhances the proliferation of both keratinocytes and fibroblasts. In keratinocytes, it reduces pro-inflammatory cytokine levels while increasing MCP-1, suggesting an anti-inflammatory effect. The decrease in  $\beta$ -catenin and E-cadherin expression promotes fibroblast migration and slows that of keratinocytes, thereby supporting normotrophic wound closure. Collectively, these results suggest that CRET may represent a promising therapeutic approach to promote wound healing with improved functional and aesthetic outcomes.

<sup>&</sup>lt;sup>2</sup>Hospital Universitario Ramón y Cajal, Servicio de Dermatología, Madrid

# Skin complications associated to peripherally inserted central catheter insertion in oncologic patients: a systematic review and meta-analysis

Larissa Santos Silva<sup>1</sup>, Ana Carolina Putini Vieira<sup>2</sup>, Ramon Huntermann<sup>3</sup>, Ana Carolina Ventura de Santana de Jesus<sup>1</sup>, Ana Clara Felix de Farias Santos<sup>4</sup>, Carolina Mira Dilly de Medeiros<sup>5</sup>, Vitoria Castro Ferreira de Oliveira<sup>6</sup>, Monaly Ribeiro\*<sup>7</sup>

**Introduction & Objectives:** Peripherally inserted central catheters (PICCs) are commonly used in oncology to deliver chemotherapy and other intravenous therapies over extended periods. While generally considered safe, PICCs can lead to complications, including skin-related issues such as infections, dermatitis, and mechanical injuries. These risks are heightened in cancer patients due to factors like advanced age, fragile skin, and treatment-related immunosuppression. Despite these risks, the frequency and nature of PICC-associated skin complications in oncologic populations remain poorly defined. This meta-analysis aims to estimate the incidence of skin complications associated with PICC use in oncology patients, offering a clearer understanding of their clinical impact.

**Materials & Methods:** We searched PubMed, Embase, and Cochrane databases up to November 2024 for randomized controlled trials and observational studies evaluating oncologic patients using PICCs. Studies were eligible if they reported at least one skin complication, including infections, allergies, mechanical or moisture-related lesions, bleeding, or pain. Statistical analyses were performed using R studio. Pooled incidence estimates were calculated with 95% confidence intervals (CIs), and heterogeneity across studies was assessed using the I<sup>2</sup> statistic. In cases of substantial heterogeneity, subgroup and leave-one-out sensitivity analyses were conducted.

**Results:** 21 studies were included, comprising a total of 4,870 oncologic patients with PICCs, of whom 206 experienced skin infections. The pooled incidence of skin infection was 3.74% (95% CI: 2.57–5.08;  $I^2 = 73.7\%$ ; p < 0.0001). Leave-one-out sensitivity analysis confirmed the robustness of the estimate (4%; 95% CI: 3–5%), and no significant publication bias was detected (Egger's test p = 0.3488). Subgroup analyses addressed specific skin-related complications. Skin allergy, assessed in three studies, showed a pooled incidence of 1.15 per 100 observations (95% CI: 0.00–4.80;  $I^2 = 92.5\%$ ). Pain associated with PICC insertion was reported in three studies, with a combined incidence of 5.86 per 100 observations (95% CI: 0.57–15.67;  $I^2 = 94.7\%$ ). Moisture-related skin lesions were evaluated in five studies, yielding a pooled incidence of 13.63 per 100 observations (95% CI: 2.43–31.03;  $I^2 = 94.7\%$ ). Mechanical skin injuries, analyzed in four studies, had a pooled incidence of 11.94 per 100 observations (95% CI: 7.32–17.49;  $I^2 = 91.1\%$ ). Lastly, bleeding complications were examined in four studies, with a pooled incidence of 1.56 per 100 observations (95% CI: 0.19–3.90;  $I^2 = 82.8\%$ ).

**Conclusion:** This meta-analysis highlights that skin complications related to PICCs are a relevant concern in oncologic patients, with notable incidences of infections, pain, dermatitis, and mechanical or moisture-related skin injuries. While most complications were mild, their frequency emphasize the need for preventive strategies and

<sup>&</sup>lt;sup>1</sup>Bahiana School of Medicine and Public Health, Salvador, Brazil

<sup>&</sup>lt;sup>2</sup>University of Santo Amaro, São Paulo, Brazil

<sup>&</sup>lt;sup>3</sup>University Center for the Development of Alto Vale, Medical Sciences Research Center, Rio do Sul, Brazil

<sup>&</sup>lt;sup>4</sup>City University of São Paulo, São Paulo, Brazil

<sup>&</sup>lt;sup>5</sup>Catholic University of Brasília, Brasília, Brazil

<sup>&</sup>lt;sup>6</sup>Federal University of Piauí, Teresina, Brazil

<sup>&</sup>lt;sup>7</sup>Faculdade São Leopoldo Mandic, Campinas, Brazil

improved catheter care protocols tailored to this vulnerable population. The observed heterogeneity suggests variability in clinical practice and reinforces the importance of consistent reporting and further research. Clinicians should remain vigilant for cutaneous adverse events in cancer patients receiving PICCs to optimize outcomes.

# Impact of senescence on mesenchymal stromal cells functionality and restoration of their migration capacity with blackbee honeys

selma Ben hammamia\*<sup>1, 2</sup>, Margot Tertrais<sup>2</sup>, Carine Nizard<sup>1</sup>, karl pays<sup>1</sup>, Robin Kurfurst<sup>1</sup>, Cécilia Brun<sup>1</sup>, Valérie Planat<sup>2</sup>

<sup>1</sup>LVMH Recherche - Hélios, Saint-Jean-de-Braye, France

# **Introduction & Objectives:**

Mesenchymal stromal cells (MSCs) include multipotent stem cells capable of differentiating into various cell types as well as connective tissue cells possessing immunomodulatory and regenerative properties. MSCs senescence is an important biological phenomenon that can limit their effectiveness during aging as well as skin repair. Therefore, it is crucial to find ways to maintain/restore their essential functions, such as migration, to maximize their repair properties.

### **Materials & Methods:**

Our study focuses on the senescence of mesenchymal stromal cells and their abilities to proliferate, differentiate, and migrate in the context of skin repair and regeneration. MSCs senescence was induced *in vitro* with a cocktail of sodium nitrite and hydrogen peroxide. High-throughput imaging techniques were used to characterize cellular senescence and analyze morphological changes, as well as adipogenic differentiation capacity. Cytokine release was evaluated through ELISA approach. Finally, migratory capacities were assessed using directed migration assays. This allowed the quantification of cell mobility through a porous membrane in response to the presence of chemo-attractants that mimic the recruitment signals of MSCs. Based on their known bioactive properties, blackbee honeys from Norway, Ouessant or Ireland and their combinations were selected to evaluate their effects on the migratory capacities of senescent MSCs.

## **Results:**

Our results validate that our chemical stress effectively induces senescence of MSCs. Indeed, the cells subjected to this chemical treatment exhibited hallmarks of senescence: proliferation arrest, resistance to apoptosis, p16 and gammaH2AX staining, and an increase in cell size and granularity along with an increased pro-inflammatory cytokine production. Those senescent MSCs displayed a loss of functionality with reduced migratory capacities. Additionally, specific honeys or their combinations were shown to improve the migratory capacities of senescent MSCs. Such mobilization was observed under conditions mimicking the recruitment of MSCs to a dermal injury site.

# **Conclusion:**

The study shows that honeys can effectively improve the migratory capacities of senescent MSCs. This improvement can be crucial for their role in skin repair and regeneration, opening to potential applications for skin interventions. The results pave the way for new strategies to use black bee honeys in the treatment of conditions related to cellular senescence and tissue regeneration.

<sup>&</sup>lt;sup>2</sup>RESTORE, Toulouse, France

# LMWH-Associated Skin Necrosis in Heparin-Induced Thrombocytopenia Type II: A Case Requiring Complex Interdisciplinary Wound Management

Simon Waigand\*1, Julia Winkler1

<sup>1</sup>Hautklinik: Universitätsklinikum Heidelberg, Heidelberg, Germany

# **Introduction & Objectives:**

Skin necrosis caused by low molecular weight heparin (LMWH) is rare but potentially life-threatening. Pathophysiological mechanisms include platelet activation via anti-PF4/heparin antibodies, as in heparin-induced thrombocytopenia type II (HIT II), immune complex deposition in dermal vessels consistent with a localized type III hypersensitivity reaction of the Arthus type, and prolonged local drug exposure in poorly perfused subcutaneous fat. In HIT II, skin necrosis occurs in up to 20% of cases with unfractionated heparin; reports under LMWH are rare. We present a case of LMWH-induced skin necrosis in an elderly patient with high clinical probability of HIT II, confirmed by serologic and functional testing, and managed through complex interdisciplinary wound care.

#### Materials & Methods:

An 83-year-old woman was referred with necrotic plaques on both upper thighs and the lower left abdomen, localized to prior LMWH (enoxaparin) injection sites. These were administered during hospitalization for a cervical burst fracture. The skin lesions developed 7–10 days after LMWH initiation, initially presenting as painful hemorrhagic bullae.

Laboratory results from the referring hospital showed a >50% decrease in platelets, from 462 G/L to 231 G/L on day 5 of LMWH administration. Despite this marked thrombocytopenia, no further diagnostic evaluation was initiated, and spinal surgery was performed. Anticoagulation was empirically switched to fondaparinux.

On admission, extended diagnostics were performed. Based on clinical presentation and timing, the 4Ts score was calculated as 8 out of 8, indicating high pretest probability for HIT II. Anti-PF4/heparin ELISA and a functional heparin-induced platelet activation (HIPA) assay confirmed the diagnosis of HIT II-associated skin necrosis.

### **Results:**

Thrombosis screening via duplex sonography and CT angiography ruled out deep vein thrombosis and pulmonary embolism. Fondaparinux was continued for three months, and the patient received a medical alert card for lifelong heparin avoidance.

Initial conservative wound care involved dry dressings on non-exudative necrotic plaques. As the condition progressed to moist necrosis, surgical debridement was performed. Given the extent of tissue damage, plastic surgery performed en bloc resection and initiated bilateral VAC therapy on the thighs. The abdominal lesion was managed by secondary wound healing. The patient required four surgical revisions due to recurrent wound bleeding. After five weeks of VAC therapy, the right thigh was closed by primary suturing. On the left, a pedicled transposition flap was used for soft tissue coverage. The patient was discharged after nearly nine weeks of inpatient care.

**Conclusion:** This case reinforces the need to recognize skin necrosis as a manifestation of HIT II. In suspected cases, the 4Ts score should guide further testing. Immediate discontinuation of heparin, lifelong avoidance, and

initiation of non-heparin anticoagulants such as danaparoid, argatroban or fondaparinux are essential to prevent thrombotic complications. In the context of complex wound care, multidisciplinary management is key to minimizing morbidity and ensuring timely surgical intervention.

# Randomised Phase 3 trial of spesolimab in patients with ulcerative pyoderma gangrenosum: A study protocol

Mark G. Lebwohl<sup>1</sup>, Alex G. Ortega-Loayza<sup>2</sup>, Arash Mostaghimi\*<sup>3</sup>, Angelo V. Marzano<sup>4, 5</sup>, Lars E. French<sup>6, 7</sup>, Keiichi Yamanaka<sup>8</sup>, Marianne Logger<sup>9</sup>, Hui Wang<sup>10</sup>, Mabrouk Elgadi<sup>11</sup>

<sup>1</sup>The Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York City, NY, United States

**Introduction & Objectives:** Pyoderma gangrenosum (PG) is a rare, inflammatory, neutrophilic dermatosis, usually manifesting as rapidly progressive and painful skin ulcers, although rarer, atypical presentations exist. Interleukin-36 (IL-36) is thought to play a key role in PG pathogenesis.1 This randomised, placebo-controlled, multicentre, Phase 3 study will assess spesolimab, a novel, humanised monoclonal antibody against the IL-36 receptor, in patients with ulcerative PG who require systemic therapy (NCT06624670). The trial has been approved by independent ethics committees of participating centres.

Materials & Methods: Approximately 90 participants aged ≥18 years with a confirmed diagnosis of ulcerative PG, from 21 countries, will be included. In Part 1 of the trial (Weeks 0–26), participants will be randomised 2:1 to receive spesolimab plus low-dose oral corticosteroid (n=60), or placebo plus low-dose oral corticosteroid (n=30) (Figure 1). In Part 2 of the trial (Weeks 28–52), participants with a non-complete response will receive spesolimab; those with a complete response will be re-randomised 1:1 to receive either spesolimab or placebo. The primary endpoint is complete closure and re-epithelisation (PGAR-100) of the target ulcer up to Week 26, confirmed ≥2 weeks later. Secondary endpoints include PGAR-100 of the target ulcer at Week 26 and of any measurable ulcer at any time up to Week 26, confirmed ≥2 weeks later. Additional efficacy, safety and biomarker measures will also be assessed.

Results: The trial started in January 2025, with estimated trial completion in October 2026.

**Conclusion:** These results will provide safety and efficacy data on spesolimab as a potential treatment for ulcerative PG.

## Reference:

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<sup>&</sup>lt;sup>2</sup>Oregon Health & Science University Hospital, Portland, OR, United States

<sup>&</sup>lt;sup>3</sup>Brigham and Women's Hospital, Boston, MA, United States

<sup>&</sup>lt;sup>4</sup>Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

<sup>&</sup>lt;sup>5</sup>Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy

<sup>&</sup>lt;sup>6</sup>Department of Dermatology and Allergy, Ludwig-Maximilians University (LMU) Hospital, Munich, Germany

<sup>&</sup>lt;sup>7</sup>Dr. Philip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, United States

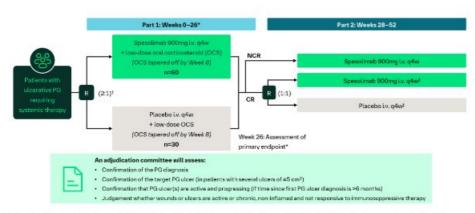
<sup>&</sup>lt;sup>8</sup>Department of Dermatology, Mie University Graduate School of Medicine, Tsu, Japan

<sup>&</sup>lt;sup>9</sup>Boehringer Ingelheim (Canada) Ltd./Ltée, Burlington, ON, Canada

<sup>&</sup>lt;sup>10</sup>Boehringer Ingelheim (China) Investment Co., Ltd, Shanghai, China

<sup>&</sup>lt;sup>11</sup>Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, CT, United States

Figure 1. Study design



"Confirmation of primary endpoint will occur at Week 28. Randomisation stratified by target PG utcer size categories (<40 cm² and >40 cm²) and presence of associated underlying inflammatory disease at baseline. This participants who experience disease recurrence in the randomized doubte-billed at ms in Part 2 can be offered open label spessioned 500 mg tx. q4w at the time of recurrence. R. complete response (i.e. complete closure of all PG utbess): iv, intravenous RCR non-complete response; CCS, one conficostero d; PG, pyaderna gangrenos.mg q4w, every 4 weeks; R, randomisation.

## The emotional impact of pyoderma gangrenosum (PG): Real-world experience of the PG patient journey

Afsaneh Alavi\*<sup>1</sup>, Dave DePottie<sup>2</sup>, Valentina Dini<sup>3</sup>, Robert S. Kirsner<sup>4</sup>, Juan Semeco<sup>5</sup>, Alex G. Ortega-Loayza<sup>6</sup>

**Introduction & Objectives:** PG is a rare, painful ulcerative neutrophilic disorder that significantly impacts patients' physical, emotional and psychosocial well-being. However, due to the rarity of PG, data are limited describing the emotional challenges faced by patients and their caregivers. This qualitative research study explored the PG patient journey, highlighting the emotional burden at each stage and the critical need for support.

Materials & Methods: Between August and September 2024, adults with PG and their caregivers were recruited through several routes, including patient advocacy groups and referrals from healthcare professionals (HCPs). Participants completed tasks on an online platform, followed by either an online 60-minute individual interview or a 90-minute interview involving 2 patients. An independent market research agency conducted the interviews and collated the data. Diagnosis by an HCP was confirmed through a pre-screening questionnaire. During the interviews, participants were asked about their experiences across different stages of their PG journey, with a particular focus on the emotional and psychosocial impact.

**Results:** In total, 22 PG patients and 4 caregivers (N=26) from the US, China, Japan and France participated in this study. Overall, 74% of PG patients were women, the majority were aged 26–55 years, 70% had been diagnosed with PG 1–5 years ago, 42% had comorbid conditions, and the majority (61%) had moderate to severe PG (self-reported). Participants reported the substantial emotional impact of PG on daily life across different stages of their PG journey (Figure 1).

Onset of symptoms: PG initially presents as a 'small bump', which grows aggressively into an ulcer, causing excruciating pain. Patients reported feeling worried, anxious, depressed and isolated as symptoms progressed.

Presentation: Patients reported experiencing high levels of distress due to the size of the ulcer, severe pain, immobilisation and difficulty performing daily tasks. They explained that PG takes over their lives, forcing them to change their routines and wardrobe, affects their ability to socialise and undertake previously loved hobbies, and impacts on relationships with family and friends. Comorbid conditions may cause delays in presenting to a dermatologist.

Diagnosis: Patients commonly reported misdiagnosis due to HCP unfamiliarity with PG. Patients reported feeling helpless and afraid, and struggling with uncertainty due to feelings of frustration, mistrust and neglect over the lack of a clear explanation of the disease by HCPs.

Treatment: PG can cause patients to stop working, leading to financial issues, which may impact treatment options. Patients conveyed feelings of isolation and pessimism when treatment options did not help relieve pain

<sup>&</sup>lt;sup>1</sup>Department of Dermatology, Mayo Clinic, Rochester, MN, United States

<sup>&</sup>lt;sup>2</sup>Patient author, Myrtle Beach, SC, United States

<sup>&</sup>lt;sup>3</sup>Dermatology Unit, Department of Clinical and Experimental Medicine, Ospedale Santa Chiara, Pisa, Italy

<sup>&</sup>lt;sup>4</sup>Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, United States

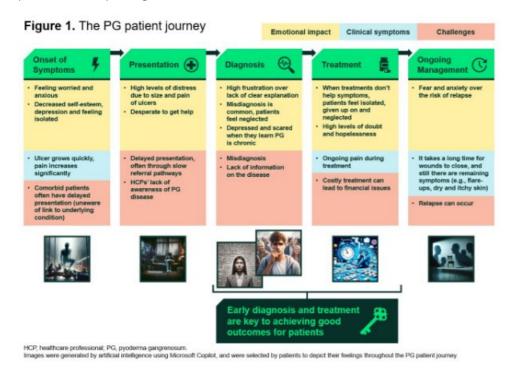
<sup>&</sup>lt;sup>5</sup>Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany

<sup>&</sup>lt;sup>6</sup>Department of Dermatology, Oregon Health and Science University, Portland, OR, United States

and symptoms, with emotions fluctuating due to the uncertainty of treatment success and impact on quality of life.

Ongoing management: Pain continues throughout treatment until wound closure, which takes a long time, causing distress. Patients also reported anxiety and a fear of the risk of relapse.

**Conclusion:** This study emphasises the substantial emotional impact of PG on patients and caregivers, and highlights their challenges throughout the patient journey. Addressing the core issue of delayed or misdiagnosis through improved disease education and offering mental health and peer support are crucial to empowering patients and improving their emotional and clinical outcomes.



# Dose and time dependent efficacy of vilobelimab on wound healing outcomes in patients with ulcerative pyoderma gangrenosum – findings from a Phase 2 trial

Afsaneh Alavi\*<sup>1</sup>, Benjamin Kaffenberger<sup>2</sup>, Robert Kirsner<sup>3</sup>, Jacek Szepietowski<sup>4</sup>, Niels Riedemann<sup>5</sup>, Camilla Chong<sup>6</sup>, Hoda Tawfik<sup>6</sup>

# **Introduction & Objectives:**

Pyoderma gangrenosum (PG) is a clinically challenging, inflammatory disorder characterized by painful, non-healing ulcers, and currently lacks approved treatments in the US or Europe. There is increasing evidence suggesting the role of human complement factor C5a in the dysregulated immune response that hinders normal healing. Vilobelimab is a first-in-class anti-C5a targeted monoclonal antibody, which specifically blocks the biological activity of C5a in human plasma with high selectivity and does not alter the membrane attack complex (C5b-9), aiming to restore immune balance and promote wound repair. This abstract highlights the wound-healing outcomes observed with escalating doses of vilobelimab in PG patients, as assessed in an international, Phase II, proof-of-concept study.

#### **Materials & Methods:**

Patients were treated biweekly in three escalating vilobelimab dosing groups of 800 mg (n=6), 1600 mg (n=6) and 2400 mg (n=7) for 26 weeks. Dose escalation to next higher dosing was allowed in patients with insufficient response at week 8 upon safety assessment of the first 4 patients per dosing group.

Wound healing was assessed using the physician global assessment (PGA) score of the target ulcer, standardized photographic documentation, the rate of wound area changes per day, the number of patients achieving >50% and 100% reduction from baseline by Day 189. Other key efficacy and patient reported outcome (PRO) endpoints were PGA score, Quality of Life and Pain measured by DLQI and NRS.

#### **Results:**

A total of 9 out of 19 patients (53%) achieved clinical remission defined closure of target ulcer assessed as PGA $\leq$ 1. Wound ulcer area decreased progressively over time. The highest dosing group (2400 mg) showed the greatest improvement, with reductions up to -90.9% (Day 189) in ulcer area healing; 6 out of 7 patients in this group achieved complete ulcer closure by study end. Across all patients,  $\geq$  50% wound area reduction was observed in 11.8% of the patients at Day 15, increasing to 77.8% of the patients by Day 189. Complete closure (100%) was seen in 0% at Days 15 and 43, and 35.7% of the patients on Day 99, and 33.3% on Day 189 with highest rates in the 2400 mg group with 85.7%) of the treated patients in this group. The mean time to target ulcer closure through all 3 dosing cohorts was 105 days.

Marked improvements were also observed in quality of life and pain, as measured by DLQI and NRS.

<sup>&</sup>lt;sup>1</sup>Mayo Clinic, Rochester, United States

<sup>&</sup>lt;sup>2</sup>The Ohio State University, Columbus, United States

<sup>&</sup>lt;sup>3</sup>University of Miami Miller School of Medicine Department of Dermatology, Miami, United States

<sup>&</sup>lt;sup>4</sup>Wrocław University of Science and Technology, Wrocław, Poland

<sup>&</sup>lt;sup>5</sup>Inflarx GmbH, Jena, Germany

<sup>&</sup>lt;sup>6</sup>InflaRx, Planegg, Germany

# **Conclusion:**

This study provides the first evidence of dose-dependent efficacy of vilobelimab in the treatment of PG, with the 2400 mg dose showing the most pronounced and consistent improvements of the PG disease shown as complete ulcer closure and reduction of pain.



Efficacy and tolerance of a prebiotic and panthenol-containing multipurpose healing dermocosmetic in infants and young children patients with superficial skin conditions: results of an international observational study

Stamatis Gregoriou<sup>1</sup>, Efstratios Vakirlis<sup>2</sup>, Malgorzata Maj<sup>3</sup>, NOHAMMED AL AYOUBI<sup>4</sup>, Emerson de Andrade Lima<sup>5</sup>, Tanongkiet Tienthavorn<sup>6</sup>, nader zaki<sup>7</sup>, Noelia Capellato<sup>8</sup>, Julio Magliano<sup>9</sup>, Kacey HAU<sup>10</sup>, Te-Peng Tseng<sup>11</sup>, Guenaelle Ledantec<sup>12</sup>, Samir Salah<sup>12</sup>, Delphine Kerob\*<sup>12</sup>

# **Introduction & Objectives:**

Children frequently experience superficial skin conditions characterized by irritation, dryness, inflammation, and minor injuries. These conditions often result from environmental factors such as irritants, temperature changes, and friction, compounded by a developing skin barrier. Such skin issues can significantly impact the quality of life for both children and their caregivers. Effective management requires gentle yet efficacious treatments suitable for pediatric use. Multipurpose healing dermocosmetic (DC) products containing prebiotic active ingredients (*Aqua Posae Filiformis*, a prebiotic complex made of ferments, sugars and plant extracts, panthenol, madecassoside, and zinc) may offer a beneficial solution for managing these pediatric skin conditions

# **Materials & Methods:**

This international observational study encompassed 16 countries and enrolled infants and young children patients presenting with superficial skin conditions. Treatment response was defined as a reduction of at least one severity grade on a five-point scale assessing the characteristic features of each condition. Clinical evaluations conducted by dermatologists, general practitioners, or pediatricians, along with caregiver assessments, were performed at baseline and at the end of the study. The Children's Dermatology Life Quality Index (cDLQI) was employed to assess the impact of these skin conditions on patients' quality of life.

# **Results:**

The study included 1,451 pediatric patients aged 10 years and under with various superficial skin conditions. The main conditions observed among the participants were dry eczematides (26.9%), non-oozing diaper rash (22.6%), unspecified irritation and cracking dermatitis (13.7%), rubbing irritation (11.0%), superficial burns (9.3%), perleche (6.7%) and vulvitis or balanitis (4.3%). The gender distribution was equal between male and female, with an

<sup>&</sup>lt;sup>1</sup>National and Kapodistrian University of Athens, Faculty of Medicine, Athens, Greece

<sup>&</sup>lt;sup>2</sup>Aristotle University of Thessaloniki, Thessaloniki, Greece

<sup>&</sup>lt;sup>3</sup>University Clinical Center of the Medical University of Warsaw, Warsaw, Poland

<sup>&</sup>lt;sup>4</sup>New Derma Clinic, Madina, Saudi Arabia

<sup>&</sup>lt;sup>5</sup>Santa Casa de Misericórdia, Recife, Brazil

<sup>&</sup>lt;sup>6</sup>Institute of Dermatology of Thailand, Bangkok, Thailand

<sup>&</sup>lt;sup>7</sup>Benha University, Benha, Egypt

<sup>&</sup>lt;sup>8</sup>Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

<sup>&</sup>lt;sup>9</sup>Universidad de la República, Montevideo, Uruguay

<sup>&</sup>lt;sup>10</sup>Derm Clinic, Hongkong, Hong Kong

<sup>&</sup>lt;sup>11</sup>Taiwan Adventist Hospital, Taipeh, Taiwan

<sup>&</sup>lt;sup>12</sup>La Roche-Posay Laboratoire Dermatologique, Levallois-Perret, France

average age of 3.5 years (SD = 2.8). The DC formulation was applied twice or thrice daily (73.3%). Lesion sizes varied, with 41.2% being between 1 and 2 cm², 47.4% between 3 and 10 cm², and 11.4% exceeding 10 cm². Following an average treatment duration of three weeks, significant improvements (P-value < 0.001) were observed across various clinical and self-reported parameters. Erythema showed improvement in 86.8% of patients, while desquamation and cracks improved in 87.2% and 88.7% of patients, respectively. Additionally, the patients exhibited significant discomfort sensations reduction, with 92.0% experiencing less burning and 90.9% experiencing less pain. The overall quality of life, as measured by the cDLQI, demonstrated a significant average improvement of 70.5%. Notably, the product exhibited a good tolerance rate of 94.0%.

#### **Conclusion:**

Daily use of the DC significantly improved superficial skin conditions in infants and young children, leading to enhanced quality of life. Clinical assessments and caregivers' evaluations revealed substantial reductions in erythema, desquamation, cracks, and discomfort sensations. The excellent tolerance profile further supports the DC formulation as a promising approach for managing pediatric superficial skin conditions.

# Integrating metabolomics and imaging data: innovative insights into the links between molecular signatures and phenotype in wound healing

Alicia Lemaire-Zady<sup>1</sup>, Eleonore GRAVIER<sup>1</sup>, Aurélie Mercadié<sup>1</sup>, Jimmy LE DIGABEL<sup>1</sup>, Pascale Bianchi<sup>1</sup>, THEUNIS JENNIFER<sup>1</sup>, Carine Jacques<sup>1</sup>, Valérie MENGEAUD<sup>2</sup>, Sandrine Bessou-Touya<sup>1</sup>, Helene Duplan\*<sup>1</sup>, Gwendal Josse<sup>1</sup>

<sup>1</sup>Pierre Fabre Dermocosmetics & Personal Care, R&D Department, Toulouse, France

# **Introduction & Objectives:**

Omics and biomedical imaging data are complementary, with omics data studying molecular mechanisms at cellular levels and imaging data describing structural or functional characteristics of tissues or organs. The integration of these two types of data (a field called "omics imaging") aims to explore links between molecular signatures provided by omics technologies (at the microscopic level) and phenotypic information provided by images (at the macroscopic level). This allows, for example, to reveal potential biological mechanisms underlying specific tissue lesions visible on biomedical images. This enhances disease understanding and treatment improvement. If common applications of omics imaging include neurology and oncology, it has not been used in dermo-cosmetics. We explored its application in wound healing to link molecular repair signatures with skin condition improvement after topical formulation use.

# **Materials & Methods:**

In a clinical study involving 21 subjects, lesions on the forearms were induced by epidermal laser ablation. The areas were then either left untreated or treated with a topical formulation containing oat Rhealba concentrate and cicahyalumide (a mixture of Rhealba, the dipeptide L-Ala-L-Glu and hyaluronic acid). Skin swabs were taken before and right after the laser ablation, on Day 5, on the re-epithelialization day (subject-dependent) and on Day 19 and were analyzed for metabolomic profiles using UHPLC-HRMS. At each sampling time, color photographs were also taken under standardized conditions using a video dermoscope camera. Twenty imaging features (colorimetry and Haralick texture features) were computed from these images using the scikit-image Python package. Statistical analyses of omics and imaging data were first performed independently using mixed linear models. For omics imaging analysis, we focused solely on the identification of metabolites linked to imaging features that best discriminated treated and untreated areas on Day 5. This integrative analysis was performed using the DIABLO method from the mixOmics R package.

#### **Results:**

Single imaging analysis enabled us to numerically quantify the improvement of the skin lesions following the application of the topical formulation. Integration of omics and imaging data revealed, among other interesting results, that the treated area presented a higher intensity of "sucrose" and "capric acid" metabolites. These metabolites were associated with skin showing more homogeneous textures and colors, as well as fewer contrasted structures compared to untreated skin. These results correspond to a phenotype with less inflammation, fewer crusts, a milder squamous state, and less dryness, indicating a better skin barrier reconstruction compared to untreated skin. Interestingly, sucrose and capric acid are two components that play a role in wound healing by promoting the commensal flora, thereby supporting the improvement of skin condition seen in the images.

<sup>&</sup>lt;sup>2</sup>Pierre Fabre Dermocosmetics & Personal Care, Laboratoires Dermatologiques A-DERMA, Lavaur, France

# **Conclusion:**

Integrating metabolomic data and biomedical images is an innovative approach in dermo-cosmetics. In the context of wound healing, it allowed to reveal metabolome-phenotype relationships after 5 days of application of a topical formula containing oat concentrate and cicahyalumide, allowing for a better understanding of mechanisms of action and efficacy of the topical formulation.



Cysteinamide as a Competitive Glycation Inhibitor to Prevent the Deterioration of Serum Components from Glucose-derived Reactions in Diabetes-mimicking Conditions

Nam Gyoung Ha\*1, Joon Yong Choi<sup>2</sup>, Yong Chool Boo<sup>2</sup>, Weon Ju Lee<sup>1</sup>, Jun Young Kim<sup>1</sup>

<sup>1</sup>Department of Dermatology, School of Medicine, Kyungpook National University, Daegu, Korea, Rep. of South <sup>2</sup>Department of Biomedical Science, The Graduate School, Kyungpook National University, Daegu, Korea, Rep. of South

# **Introduction & Objectives:**

Persistent hyperglycemia in diabetes promotes protein glycation and accumulation of advanced glycation endproducts (AGEs), leading to oxidative stress, inflammation, and impaired tissue repair. This study aimed to identify small molecule nutrients that inhibit glucose-induced glycation of serum components and enhance the survival and wound healing of human dermal fibroblasts (HDFs) under diabetes-mimicking conditions.

### **Materials & Methods:**

Cell culture media containing low (5.5 mM) or high glucose (50 mM) were heat-treated at 60°C for 72 h to simulate diabetic conditions. Various free and amidated amino acids and antioxidant compounds were screened. Glycation products were quantified by a fluorescence-based AGEs assay. SDS-PAGE and TLC were performed to analyze protein and small molecule modifications. HDF viability was assessed by MTT assay, and wound healing was evaluated by an in vitro scratch assay.

# **Results:**

Heat-treated high-glucose media showed increased glycation products and decreased HDF viability. Among the tested compounds, only cysteinamide (C-NH2) and its derivative N-acetylcysteinamide (NAC-NH2) effectively prevented medium deterioration, enhanced cell viability, and promoted wound healing. C-NH2 acted as a competitive glycation inhibitor, reducing serum protein glycation while forming its own glycation products. Conventional antioxidants and known glycation inhibitors such as aminoguanidine and pyridoxamine were ineffective.

#### **Conclusion:**

C-NH2 and NAC-NH2 exhibit unique protective effects against glucose-induced medium deterioration, improving fibroblast survival and wound healing in diabetic-like environments. These compounds may serve as promising therapeutic candidates for managing diabetic skin complications.

# Innovative and Simple approach for treatment of chronic ulcers with collagen fibres.

Ramesh Viswanath<sup>1, 2</sup>, ritu vishwanath<sup>1, 3</sup>, varun vishwanath<sup>4</sup>

<sup>1</sup>pratima relief institute of medical sciences, dermatology venereology and leprology, Warangal, India

**Introduction & Objectives:** Chronic ulcers are the ulcers that last for more than six weeks. They are very commonly encountered by dermatologists. Many treatment options are available, yet they are difficult to treat.

To evaluate the efficacy of collagen fibre dressings in chronic ulcers of different etiologies.

**Materials & Methods:** This is a prospective study including 20 adult patients with chronic ulcers. All the patients were examined for the underlying cause of the ulcers and started treatment for the same. They were dressed with the mixture of collagen fibres with topical antibiotics every week for 12 weeks and the response was recorded.

**Results:** Twenty patients aged 18 – 80 years (mean age 46.4 years), 10 males and 10 females presented with chronic ulcers ranging from two months to 12 months duration (mean 6.35 months). The etiologies were varicose ulcers in 7, Hansens disease trophic ulcers in 7, traumatic in 3, diabetic ulcer with maggots in 1, Vasculitic ulcer in 1 and atrophy blanche in 1 patient. The average number of dressings required were 8. Good and rapid improvement was seen. Ulcers healed completely in 80% of cases in 3 months. Duration of ulcer had positive correlation (0.46) with number of dressings. The remaining 20% required a greater number of dressings.

Conclusion: Collagen is a valid therapeutic option as a bioactive advanced dressing in chronic ulcer management.

<sup>&</sup>lt;sup>2</sup>v ramesh skin clinic, dermatology venereology and leprology, Warangal, India

<sup>&</sup>lt;sup>3</sup>riva skin and plastic surgery clinic, dermatology venereology and leprology, warangal, India

<sup>&</sup>lt;sup>4</sup>riva skin and plastic surgery clinic, plastic surgery, Warangal, India

#### A Silent Threat: MRI-Related Thermal Burn from Skin-to-Skin Contact

Sıla Serin\*<sup>1</sup>, pınar özdemir çetinkaya<sup>1</sup>, Ilknur Altunay<sup>1</sup>

<sup>1</sup>University of Health Science, Şişli Hamidiye Etfal Training and Research Hospital, Dermatology, İstanbul, Türkiye

# **Introduction & Objectives:**

Thermal injuries are the most common type of adverse event related to magnetic resonance imaging (MRI) procedures, according to Food and Drug Administration (FDA) data. Most of these events have been observed in patients to whom external metal-containing monitoring devices, such as electrocardiogram leads and pulse oximeters, were attached. Even without external devices, patients may experience thermal burns from contact with MRI radiofrequency coils or skin-to-skin contact. During MRI, skin-to-skin contact can cause the scanner to emit high-power electromagnetic radiofrequency pulses that are conducted through the body, generating heat. Tissue loops are created at points of skin-to-skin contact, thus forming a closed conducting circuit. The current flowing through this circuit can produce second-degree burns. This phenomenon has not received sufficient attention in the literature. Herein, we present a case of MRI-related thermal burn. Our aim is to highlight the risk of tissue loop-related thermal burns during MRI and to raise awareness among healthcare professionals about the importance of preventive positioning practices.

#### Materials & Methods:

A rare case of MRI-related thermal burn is presented.

# **Results:**

A 55-year-old male patient with a known history of type 2 diabetes mellitus was admitted to the plastic and reconstructive surgery clinic for management of a chronic wound on his left lower extremity. Upon admission, systemic antibiotics and vacuum-assisted closure (VAC) therapy were initiated. Meanwhile, an MRI scan was performed to rule out osteomyelitis. The patient experienced a painful burning sensation during the MRI between his thighs. Despite informing the radiology technicians, he was reassured that the sensation was not unusual, and the scan was completed. Upon returning to the inpatient unit, his daughter observed new blisters on both inner thighs that had not been present prior to the imaging. The patient was referred to the dermatology clinic, and on dermatological examination, bilateral bullous lesions were observed on the medial aspects of the thighs. The lesions were located on the areas where the medial surfaces of the thighs come into contact when the legs are brought together, appearing to "kiss" each other. Based on the patient's history, as well as the characteristics and location of the lesions, a diagnosis of an MRI-associated burn was established. We believe that during positioning in the MRI scanner, the patient inadvertently brought his thighs together, forming a closed-loop conductive circuit that led to a thermal burn. The patient was started on dexpanthenol cream, and at the follow-up visit one week later, the lesions were observed to have regressed.

## Conclusion:

This case report highlights a preventable yet often overlooked risk associated with MRI procedures. Preventing skin-to-skin contact during patient positioning and avoiding potential closed-loop formations are critical measures to reduce the risk of thermal injury. Increasing awareness among clinicians and MRI technicians can help prevent similar incidents in this widely used imaging modality.

The Joint Impact of Elevated Homocysteine and Type 2 Diabetes on Non-Healing Wounds and All-Cause Mortality: Integrated Clinical and Multi-Omics Analyses

Yichuan Li<sup>1</sup>

<sup>1</sup>Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Department of Dermatology, Wuhan

# **Introduction & Objectives:**

Hyperhomocysteinemia (HHcy) and type 2 diabetes (T2D) are recognized risk factors for non-healing wounds, yet their combined effects and underlying mechanisms remain unclear.

#### **Materials & Methods:**

In this study of 8406 NHANES participants (1999-2004), weighted logistic regression was used to estimate odds ratios for non-healing wounds, and Cox proportional hazards models were employed to assess hazard ratios for all-cause mortality. Additive and multiplicative interactions were evaluated. Nonlinear relationships using restricted cubic splines (RCS). Mediation analyses explored inflammatory marker contributions. Bulk transcriptomic and single-cell sequencing data were integrated to identify Hcy-DFU hub genes, construct an Hcy risk gene scoring system, and elucidate key mechanisms by which Hcy remodels the DFU microenvironment.

#### **Results:**

Both T2D (OR: 2.42, 95% CI: 1.69-3.47) and HHcy (OR: 1.67, 95% CI: 1.10-2.54) independently elevated non-healing wound risk. Participants with both conditions exhibited higher odds (OR: 5.28, 95% CI: 3.20-8.70), with additive interaction (RERI: 2.83, AP: 0.54, SI: 2.95). In diabetic men, Hcy displayed a J-shaped relationship with non-healing wounds (P for nonlinearity = 0.027), with the lowest risk around 8.9 µmol/L. In diabetic patients, inflammatory markers mediated the link, with proportions of 11.1% for RDW, 9.16% for MLR, 5.28% for SIRI, and 4.03% for NLR. Hcy drove immune-metabolic reprogramming in the DFU microenvironment by regulating key gene networks such as IL1B and MMP9, activating the MIF-CD74/CXCR4 axis to form a B cell-centric inflammatory cascade network. Both T2D and HHcy were associated with higher all-cause mortality, without joint interaction observed. Participants with a history of non-healing wounds had higher all-cause mortality risk.

# **Conclusion:**

T2D and HHcy synergistically worsen non-healing wounds, but not all-cause mortality. In diabetic males, Hcy levels displayed a J-shaped relationship with non-healing wound risk. Mechanistically, Hcy amplified systemic inflammation and drove stromal-immune crosstalk via the MIF-CD74/CXCR4 axis, reshaping the diabetic wound microenvironment.

# A Complex ANA-Positive Case of Recurrent Chronic Leg Ulcers in the Absence of Confirmed Systemic Autoimmune Disease

Mariam Nikolaishvili<sup>1</sup>, Janadi Karawita<sup>2</sup>, Ani Pazhava<sup>3</sup>, Nino Kantaria<sup>2</sup>

<sup>1</sup>Ilia State University, Tbilisi, Georgia

<sup>2</sup>Medical University, Tbilisi, Georgia

<sup>3</sup>Mayo Clinic, Dermatology, Rochester, United States

# **Introduction & Objectives:**

Recurrent leg ulcers in patients who test positive for antinuclear antibodies (ANA) without a confirmed diagnosis of systemic autoimmune disease pose significant diagnostic and therapeutic challenges. These instances occur at the confluence of dermatology, rheumatology, and hematology, where clinical manifestations indicate the possibility of systemic involvement but do not fulfill the criteria for established classification. We present a complex case involving a 40-year-old female with a protracted history of autoimmune thyroiditis and recurrent ulcerations of the lower extremities, which raises concerns for potential connective tissue disease, pyoderma gangrenosum, or an unspecified vasculopathy.

# **Materials & Methods:**

The patient, diagnosed with autoimmune thyroiditis at age 13, has been ANA-positive (1:320) since her early 30s. She experienced livedo reticularis and Raynaud's phenomenon prior to developing chronic, relapsing leg ulcers, initially affecting the right leg and subsequently both lower limbs. Over the past decade, investigations included CT angiography (showing mesenteric inflammation and lymphadenopathy), lymph node biopsy (confirming benign lymphadenopathy), extensive autoimmune serologies (all negative except ANA), and evaluation for thrombocytosis and leukocytosis.

Therapeutic trials incorporated enoxaparin, aspirin, vasodilators (Vasoprostane), hydroxychloroquine, and various surgical interventions, including punch skin grafting. Infectious disease specialists proposed a diagnosis of pyoderma gangrenosum, and systemic steroids were recommended but declined. No skin biopsy has been conducted on either ulcerated or healthy tissue. Rheumatologists ruled out SLE and attributed ANA positivity to thyroiditis, despite considering systemic lupus as a differential diagnosis.

#### **Results:**

The ulcers responded partially to anticoagulation and improved during pregnancy-associated immunologic shifts, but consistently relapsed postpartum. The most recent ulcer (2024) on the left medial malleolus is large, irregular, hyperemic, and exudative, with granulation tissue and fibrin. A new lesion is forming on the contralateral foot. Hydroxychloroquine improved Raynaud's but did not prevent ulcer recurrence. ANA titer remains stable, with no emergence of other autoimmune markers.

# Conclusion:

This case underscores the clinical intricacies associated with patients who test positive for antinuclear antibodies (ANA) and suffer from chronic leg ulcers in the absence of systemic autoimmune confirmation. The patient exhibits overlapping characteristics indicative of livedoid vasculopathy, pyoderma gangrenosum, and lupus profundus, all the while not meeting the full diagnostic criteria for any singular condition. A diagnostic skin biopsy

is scheduled to elucidate the underlying etiology. Collaborative efforts across multidisciplinary teams are crucial in such ambiguous presentations to circumvent diagnostic inertia and enhance targeted management.

# Before amputating, consult a dermatologist: Pyoderma gangrenosum mimicking necrotizing fasciitis

Luis Felipe Godoy Villalón\*<sup>1</sup>, Andrea San José Rodríguez<sup>2</sup>, Gabriel Rodríguez Vega<sup>2</sup>, Elia Diaz Torres<sup>2</sup>, Julio Rodríguez López<sup>2</sup>, Francisco Granados Pacheco<sup>3</sup>, Laura Rodríguez-Lago<sup>2</sup>, maria zaida hernandez hernandez<sup>2</sup>

<sup>1</sup>Complejo Hospitalario Universitario Insular Materno-Infantil, Dermatology, Las Palmas de Gran Canaria, Spain <sup>2</sup>Complejo Hospitalario Universitario Insular Materno-Infantil, Dermatology, Las Palmas De Gran Canaria, Spain <sup>3</sup>Complejo Hospitalario Universitario Insular Materno-Infantil, Pathological anatomy, Las Palmas De Gran Canaria, Spain

**Introduction & Objectives:** Pyoderma gangrenosum (PG) is a neutrophilic dermatosis often associated with systemic diseases and pathergy phenomenon. It can rarely complicate surgical procedures, potentially leading to unnecessary debridement and morbidity.

**Materials & Methods:** A 23-year-old male with oculocutaneous albinism underwent arthroscopic cruciate ligament reconstruction in the left knee. Postoperatively, he developed fever, pain, functional limitation, and dehiscence with purulent discharge from surgical wounds. Septic arthritis was suspected, and he was hospitalized and started on antibiotics. The clinical course was poor, with persistent fever, tachycardia, and elevated acutephase reactants despite multiple surgical debridements. Due to refractory shock and extensive tissue necrosis, a supracondylar amputation was performed.

A diagnosis of necrotizing fasciitis was made, and antibiotic therapy and surgical management were intensified. However, the condition worsened, with progressive skin loss and persistently negative cultures.

Subsequently, new ulcers developed around vascular access sites in the upper limbs, prompting a dermatology consultation. Physical examination revealed rounded ulcers with central slough, purulent exudate, and undermined violaceous borders on the left forearm and right arm, as well as similar features on the amputation stump. Histopathology showed dense neutrophilic infiltrates in both the ulcers and the stump, with negative cultures. A diagnosis of PG was made, and high-dose corticosteroids, cyclosporine, and optimized wound care were initiated, resulting in rapid clinical, laboratory, and dermatological improvement. The stump was eventually closed, and the patient is currently undergoing rehabilitation.

**Results:** Post-surgical PG is a rare complication triggered by pathergy phenomenon. It can occur after various surgical procedures and could lead to unnecessary procedures. In 2019, Sanchez et al, coined Necrotizing neutrophilic dermatosis (NND) to refer cases of PG or Sweet syndrome associated with prominent systemic inflammation, such us, fever, elevated markers of inflammation or shock. NND could mimic severe infections such as necrotizing fasciitis or septic shock, To date, there has been a total of 45 cases of PG mimicking necrotizing fasciitis published in the literature. Recognizing these cases is crucial to avoid unnecessary surgical interventions, such as debridement or even amputation, which may worsen the condition. Few cases have been reported where diagnostic delays led to limb amputation, as in our patient.

In uncertain cases, histopathological examination and tissue cultures are mandatory. While awaiting diagnostic confirmation, the early initiation of immunosuppressive therapy may be beneficial, particularly in critically ill patients with multiple negative cultures who do not respond to antibiotic treatment.

**Conclusion:** This case highlights the importance of considering dermatologic evaluation in cases of soft tissue infections with atypical or poor progression. Early identification of PG can prevent unnecessary procedures such as

repeated debridement or even amputation.

# Monitoring Chronic Wounds with a Bioimpedance-Based Method: A Systematic Review and Case Report

Magdalena Antoszewska\*<sup>1</sup>, Piotr Spychalski<sup>2</sup>, Atte Kekonen<sup>3</sup>, Jari Viik<sup>3</sup>

- <sup>1</sup>Medical University of Gdańsk, Department of Dermatology, Venereology and Allergology, Gdańsk
- <sup>2</sup>Medical University of Gdańsk, Department of General, Endocrine and Transplant Surgery, Gdańsk
- <sup>3</sup>Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

# **Introduction & Objectives:**

Chronic wounds reduce patients' quality of life and impose a significant economic burden on healthcare systems. Bioimpedance-based methods show promise for monitoring wound healing. This review explores the literature on bioimpedance in wound care and presents preliminary results from a clinical trial assessing the feasibility and effectiveness of a new bioimpedance-based system for monitoring venous ulcer healing.

#### **Materials & Methods:**

A systematic review of the literature was conducted following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines across three electronic databases: PubMed, Scopus, and Web of Science. For the clinical trial, a patient with a chronic lower extremity ulcer caused by venous insufficiency participated. Wound healing was monitored during regular visits to a Surgical Outpatient Clinic, using a monitoring method based on quasimonopolar bioimpedance measurements. The patient attended two study visits per week until the ulcer fully healed.

# **Results:**

Sixteen studies were included in the review, highlighting various approaches to using bioimpedance for monitoring wound healing. The results showed a consistent increase in bioimpedance as the ulcer's surface area decreased. A strong, statistically significant negative correlation was observed between bioimpedance values and wound size, indicating that as the wound healed, bioimpedance measurements rose accordingly.

# **Conclusion:**

In conclusion, bioimpedance-based methods offer a promising and non-invasive approach for monitoring the wound healing process.

# Impact of malodor on health-related quality of life (HRQoL) of patients with chronic wounds due to volatile organic compounds (VOCs)

Ewa Klara Stuermer\*<sup>1</sup>, Clara Nathrath<sup>1</sup>, Henrick Lober<sup>2</sup>, Toni Janke<sup>3</sup>, Stefanie Sielemann<sup>2</sup>, Matthias Augustin<sup>3</sup>, Sophie Charlotte Liegenfeld<sup>1</sup>

<sup>1</sup>University Medical Center Hamburg-Eppendorf, Comprehensive Wound Center, Department for Vascular Surgery, Hamburg, Germany

<sup>2</sup>Hamm-Lippstadt University of Applied Sciences, Hamm, Germany

<sup>3</sup>University Medical Center Hamburg-Eppendorf, Institute for Health Services Research in Dermatology and Nursing (IVDP), Hamburg, Germany

# **Introduction & Objectives:**

Chronic wounds significantly impact health-related quality of life (HRQoL). Unpleasant wound odor, caused by bacterial colonization and necrotic processes, is a distressing symptom. Its exact composition is not well understood, but it could be the basis for a personalized odor avoidance strategy.

#### Materials & Methods:

Therefore, this feasibility study explored 92 wounds from 66 patients with the focus on wound odor, bacterial burden and their impact on health related-quality of life (HRQoL). Volatile organic compounds (VOCs) responsible for wound odors were detected at the molecular level, using gas chromatography-mass spectrometry and -ion mobility spectrometry and correlated to the HRQoL.

# **Results:**

In patients analyzed (average age 69±13 years, wound persistence 24.31±70.8 months) 135 pathogens were identified by swabbing including 19% *Staphylococcus aureus*, 15% *Pseudomonas aeruginosa*, and 35% Enterobacteria. The specific questionnaire "Wound-QoL-14" showed a non-significant difference in HRQoL in patients with wound odor (2.1±1.0 vs. 1.8±1.0). The latter also had the highest number of VOC detections. The most frequently detected, relevant VOCs from prokaryotic sources were dimethyl-disulfide and diacetyl-(2,3-butanedione). Furthermore, potential biomarkers for specific pathogens were identified, including dimethyl-trisulfide for *P. aeruginosa* and indole for *E. coli*. The most prevalent substance groups were ketones and alcohols. In conclusion, the malodor of chronic wounds is caused by a mixture of the intrinsic odor of bacterial products and necrosis.

# Conclusion:

This exploratory study, which combines the analysis of decoded VOCs and the olfactory assessment of odor, could be a novel, targeted approach for identifying potential "anti-wound odor therapies" that will significantly benefit the HRQoL of patients with malodorous tumor wounds, in particular.

# Pathogenic and non-pathogenic microbes in the skin and wound microbiome - How to flip the switch?

Ewa Klara Stuermer\*<sup>1</sup>, Julian-Dario Rembe<sup>2</sup>, Mandy Dittmer<sup>1</sup>, Paulo Ramos<sup>3</sup>, Sophie Charlotte Liegenfeld<sup>1</sup>

<sup>1</sup>University Medical Center Hamburg-Eppendorf, Comprehensive Wound Center, Hamburg, Germany <sup>2</sup>University Hospital Duesseldorf (UKD), Heinrich-Heine-University (HHU) Duesseldorf, Department of Vascular and Endovascular Surgery, Düsseldorf, Germany

<sup>3</sup>Universidade Católica Portuguesa, Oporto Campus, Institute of health Science, Nursing Department, Oporto, Portugal

# **Introduction & Objectives:**

Chronically infected wounds are a complex healthcare problem and their incidence has been steadily increasing over the past decades. The wound microbiome plays a central role in wound pathology: the ratio of pathogenic and commensal bacteria in a wound has a decisive influence on the healing process. Recent research on the skin microbiome shows that it can be modulated by targeted interventions, such as altering pH or using probiotics, to positively influence the dysregulated regeneration processes in dermatological conditions.

# **Materials & Methods:**

A systematic literature review was performed by including studies published in the last ten years (2014-2024). The following keywords were included: "wound microbi-ome", "complex wounds" and microbiome, "acute wounds" and microbiome, probiotics and "wound microbiome", probiotics and "chronic wound", probiotics and "wound healing", and "chronic wounds" and antiseptics. Keywords were combined using the Boolean operators "and" and "or". Out of the 517 articles obtained after entering the keywords into the search engine, 27 were duplicates and 259 were excluded based on the exclusion criteria.

#### **Results:**

The following findings were extracted: The composition of the wound microbiome varies according to site, cause, genetic predisposition and (social) environment. A healthy skin microbiome can promote healing, whereas an imbalance between pathogenic and symbiotic microorganisms contributes to infection or even chronicity in dermatological diseases and wounds. Current treatments for infected skin and wounds include antiseptics and antibiotics. Their non-specific use targets both pathogenic and commensal bacteria, further exacerbating the existing imbalance in the skin microbiome. Commensal bacteria of the skin microbiome, such as *Staphylococcus epidermidis*, *Acinetobacter lwoffii* and *Staphylococcus lugdunensis*, can specifically help fight pathogens, restore balance and promote wound healing through competitive growth and direct inhibition.

# **Conclusion:**

Understanding of the skin and wound microbiome and its complex interactions is critical in skin disease, particularly in wound healing. The targeted use of probiotics could become a valuable tool in the treatment of atopic skin diseases and wounds.

# When Paresthesia Leads to Ulceration: Two Cases of Trigeminal Trophic Syndrome

Fouad Mohamed Amine<sup>1</sup>, Nesrine Ben Salah<sup>1</sup>, soua yousra<sup>1</sup>, bel hadj ali hichem<sup>1</sup>, youssef monia<sup>1</sup>, zili jamel<sup>1</sup>

 $^{1}$ مستشفى فطومة بورقيبة بالمنستير, Dermatology Department, Monastir, Tunisia

# **Introduction & Objectives:**

Trigeminal trophic syndrome (TTS) is a rare neurocutaneous disorder characterized by the trigeminal nerve dysfunction (anesthesia/hypoesthesia), chronic paresthesia, and ulcerative lesions within the affected dermatome. Pathophysiology involves a vicious cycle of sensory loss, abnormal sensations, and self-inflicted trauma due to unconscious manipulation. We present two paradigmatic cases illustrating the diagnostic challenges and multidisciplinary management approach required for this condition.

#### Materials & Methods:

NA

#### **Results:**

Our first case involved a 52-year-old woman with a history of Wallenberg syndrome secondary to left vertebral artery occlusion four years prior. She developed persistent ulcerations on the left V1/V2 dermatomes over six months, featuring characteristic well-demarcated, crescent-shaped ulcers with necrotic bases and raised violaceous borders. Neurological examination revealed diminished pinprick and temperature sensation in the affected areas, while light touch and vibration sense remained intact. The second case was a 64-year-old man who presented with nearly identical ulcerations in the left V1 distribution, developing four years after ophthalmic herpes zoster infection. Both patients demonstrated unconscious rubbing behaviors during clinical observation. Histopathological examination in both cases showed non-specific ulceration with absent neutrophilic infiltrates, ruling out vasculitic or infectious processes. Comprehensive workup including hematological, biochemical, and immunological parameters was unremarkable. The female patient responded well to carbamazepine 200mg/day combined with silicone-based dressings, achieving complete healing by week 10. The male patient required pregabalin 75mg/day and temporary use of a transparent facial shield, with full re-epithelialization occurring by week 12.

# **Conclusion:**

TTS remains a diagnostically challenging condition that requires high clinical suspicion, particularly in patients with known trigeminal nerve injury. The pathogenesis involves a complex interplay between sensory denervation, subsequent paresthesia, and repetitive self-inflicted trauma, often exacerbated by impaired proprioceptive feedback. Our cases underscore two distinct etiologies, vascular and infectious, that can lead to this syndrome following variable latent periods. The therapeutic approach must address both the neuropathic component through membrane-stabilizing agents and the behavioral aspect through patient education and physical barriers. While multiple pharmacologic options exist, including gabapentin, tricyclic antidepressants, and topical capsaicin, the optimal regimen remains unclear due to the condition's rarity. These cases highlight the importance of early recognition and multidisciplinary management involving neurologists, dermatologists, and wound care specialists to prevent chronic disfiguring ulceration.

# Chronic Ulcers and Endovenous Timing: What Every Dermatologist Should Know

Ahmed Mohammad Emam Hassan<sup>1</sup>, Aya Mohamed<sup>2</sup>, Mohammed Al Abadie<sup>3</sup>

<sup>1</sup>University Hospital Coventry & Warwickshire, Vascular suregry, Coventry, United Kingdom

# **Introduction & Objectives:**

Chronic venous ulcers are among the most common leg ulcers encountered by dermatologists, often presenting in elderly patients with comorbidities. While compression therapy remains a cornerstone, dermatologists are increasingly involved in multidisciplinary wound care strategies, including referring for endovenous ablation.

# **Materials & Methods:**

We retrospectively reviewed patients with CEAP C6 venous ulcers treated from 2022 to 2024.

Two approaches were compared: - Group A: Immediate foam sclerotherapy during the same session as RFA - Group B: Delayed sclerotherapy 2–4 weeks after RFA

Outcome measures included ulcer healing time, reduction in venous clinical severity score (VCSS), complication rates, and 6-month recurrence. Dermatological follow-up included assessment of skin inflammation, pigmentation, and ulcer resolution.

#### Results:

Patients in Group A experienced significantly faster healing (6.4 vs. 9.1 weeks, p < 0.05). Dermatological signs such as stasis dermatitis and lipodermatosclerosis improved faster in the immediate group. No increase in pigmentation or post-inflammatory changes was noted in Group A. Ulcer recurrence at 6 months: 8% in Group A vs. 18% in Group B. No significant differences in adverse effects.

# **Conclusion:**

This study highlights that early intervention with foam sclerotherapy post-RFA enhances healing and minimizes dermatological sequelae such as pigmentation or induration. Dermatologists should not only identify and diagnose venous ulcers but also coordinate early referral for endovenous therapy and ensure post-procedural skin monitoring.

Immediate combined treatment of RFA and foam sclerotherapy can significantly improve dermatologic and healing outcomes in venous ulcers. Dermatologists are in a key position to guide patient pathways and follow-up care to reduce recurrence and chronic skin damage

<sup>&</sup>lt;sup>2</sup>HealthHarmonie, Dermatology, Birmingham, United Kingdom

<sup>&</sup>lt;sup>3</sup>North Cumbria Integrated Care NHS Foundation Trust, Dermatology, North Cumbria, United Kingdom

# Synergistic Effects of Essential Oils and Probiotics Against Chronic Wound Pathogens

Beatrice Balaceanu-Gurau\*<sup>1, 2</sup>, Alina Maria Holban<sup>3, 4</sup>, Cornelia-Ioana Ilie<sup>5, 6</sup>, Cristian-Dorin Gurău<sup>1, 7</sup>, Lia-Mara Diţu<sup>3, 4</sup>, Mara-Mădălina Mihai<sup>1, 2, 4</sup>

# **Introduction & Objectives:**

Alterations in the cutaneous microbiota can negatively influence wound healing processes and contribute to both acute and chronic infections. Effective infection control strategies rely on the identification of bacterial species, evaluation of antimicrobial resistance patterns, and understanding of biofilm-forming capabilities. In cases of recurrent infection, repeated antibiotic therapies are often required, which may promote the development of resistance to conventional antimicrobials. As a result, there is growing interest in alternative approaches—such as the use of essential oils and probiotics—that may offer novel and complementary strategies for infection management.

# **Results:**

We performed a laboratory-based microbiological investigation to examine the virulence traits, biofilm production capacity, and antimicrobial susceptibility of bacterial isolates obtained from chronic wound specimens. The antimicrobial potential of natural substances—including sandalwood essential oil, propolis tincture and ylang-ylang oil —and selected probiotic strains (*Lactobacillus acidophilus*, *L. plantarum*, *L. paracasei*, *Lactococcus lactis*, and *L. rhamnosus*) was evaluated.

Gram-positive bacteria displayed greater susceptibility to essential oils compared to Gram-negative counterparts. Among the tested substances, sandalwood oil, ylang-ylang oil, and propolis tincture exhibited pronounced antibacterial activity, suggesting their potential role in the topical management of cutaneous infections. Notably, sandalwood oil showed efficacy not only against Gram-positive strains but also against *Morganella morganii*, a Gram-negative species. However, the widespread use of ylang-ylang in cosmetic products may pose a risk of microbiota disruption, warranting further safety assessments.

Probiotic strains also demonstrated notable antimicrobial properties. *Lactobacillus paracasei* effectively inhibited the adhesion of Gram-positive bacteria, while *L. rhamnosus* cell suspensions significantly suppressed bacterial growth. Although additional studies are needed to explore potential synergistic effects, a combination of sandalwood essential oil with *L. rhamnosus* supernatants resulted in enhanced inhibition of Gram-positive organisms.

# **Conclusion:**

<sup>&</sup>lt;sup>1</sup>Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

<sup>&</sup>lt;sup>2</sup>Elias Emergency University Hospital, Department of Oncologic Dermatology, Bucharest, Romania

<sup>&</sup>lt;sup>3</sup>Faculty of Biology, Department of Botany-Microbiology, University of Bucharest, Bucharest, Romania

<sup>&</sup>lt;sup>4</sup>Research Institute of Bucharest, Bucharest, Romania

<sup>&</sup>lt;sup>5</sup>Department of Science and Engineering of Oxide Materials and Nanomaterials, Faculty of Applied Chemistry and Materials Science, University Politehnica of Bucharest, Bucharest, Romania

<sup>&</sup>lt;sup>6</sup>Faculty of Applied Chemistry and Materials Science, National Centre for Micro and Nanomaterials and National Centre for Food Safety, University Politehnica of Bucharest, Bucharest, Romania

<sup>&</sup>lt;sup>7</sup>Clinical Emergency Hospital, Orthopedics and Traumatology Clinic, Bucharest, Romania

The increasing prevalence of multidrug-resistant pathogens, driven in part by antibiotic overuse, represents a critical challenge in modern medicine. Understanding biofilm dynamics and developing strategies for their disruption are essential for advancing chronic wound care. Essential oils represent a promising class of antimicrobial agents, but their safety, formulation, and clinical application must be carefully standardized. The incorporation of probiotics, either alone or in combination with plant-based compounds, may offer an innovative path toward more effective and sustainable infection control strategies.

# **Hospital Prescription of Advanced Wound Dressings: Impact on Outpatient Costs**

kazuma terashi<sup>1</sup>, Kenny Velia\*<sup>2</sup>, Jean-Luc Perrot<sup>2</sup>, Manon Benmalek<sup>1</sup>, Odile Nuiry<sup>1</sup>

<sup>1</sup>CHU Saint-Etienne, Hôpital Nord, Pharmacy, Saint-Priest-En-Jarez, France

# **Hospital Prescription of Advanced Wound Dressings: Impact on Outpatient Costs**

# **Introduction & Objectives:**

In 2024, the French Social Security deficit reached €15.3 billion, including €13.8 billion for the healthcare branch. Although this figure is lower than the initially projected €18.2 billion, it represents a deterioration compared to 2023 (€10.8 billion). This trend underscores the importance of enhancing healthcare efficiency to control health expenditures.

This study assesses the impact of advanced wound dressings (AWDs) prescribed at hospital discharge on outpatient healthcare costs.

#### Materials & Methods:

Data from the French National Health Data System (SNDS: système national des données de santé) were extracted for the year 2024 in .xls format. They are transmitted to healthcare institutions by social health insurance. Only outpatient dispensations directly attributable to our university hospital were included. Dressings were classified by type: hydrocellular, hydrocolloid, alginates (including 'pure' alginates as defined in the official reimbursement list), charcoal, hydrofiber, interfaces, sterile greasy gauze, hydrogels, and matrix metalloproteinase inhibitors. Classes with fewer than 10 units dispensed were excluded.

# **Results:**

In 2024, our institution was responsible for the outpatient dispensation of 36,869 boxes of dressings, totaling €964,397. Hydrocellular dressings were the most prescribed, accounting for 73.8% of boxes dispensed and €624,992 in costs, including €71,421 for anatomically adapted forms (e.g., heel, sacrum).

Pure alginates ranked second in volume (5.6%) and generated €100,418 (10.2% of costs). Dressings with matrix metalloproteinase inhibitors, though representing only 3.4% of units, accounted for €98,653 (9.5%).

Conversely, 'classic' alginates made up just 0.3% of volumes and €1,726 in costs.

#### **Conclusion:**

At the level of a university hospital, advanced wound dressings prescribed at discharge account for nearly €1 million annually in community healthcare expenditures, with hydrocellular dressings representing the largest share (>60%).

These data, still often overlooked by prescribers, highlight the importance of rational and evidence-based

<sup>&</sup>lt;sup>2</sup>CHU Saint-Etienne, Hôpital Nord, Dermato-allergo-oncologie, Saint-Priest-En-Jarez, France

prescribing. Targeted awareness among medical teams is essential to control costs while maintaining the quality of care.

Soon, these community expenditures are expected to be incorporated into hospital budget responsibility, as foreseen by upcoming healthcare financing reforms. Therefore, addressing outpatient prescription costs also means anticipating the future financial burden on hospital departments.

It is essential for hospital prescribers to adopt a similar accountability mindset to that of private practitioners, who can monitor their prescribing impact through French national health insurance prescribing data system reports (SNIR: système national inter-régime).

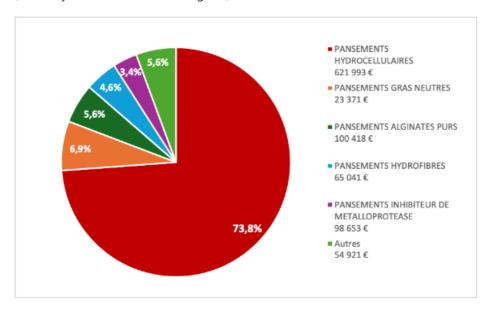


Figure: Distribution of advanced wound dressings prescribed at hospital discharge in 2024 (by percentage of boxes dispensed) and associated cost (€).

The "Other" category includes interface dressings (2.4%), hydrogels (1.6%), hydrocolloids (1.3%), classic alginates (0.3%), and charcoal dressings (0.1%).



A systematic review of procedural treatments for burn scars in children: Evaluating efficacy, safety, standard protocols, average sessions and tolerability based on clinical studies

Alireza Jafarzadeh\*<sup>1</sup>, azadeh goodarzi<sup>1</sup>

<sup>1</sup>Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran , Tehran, Iran

# **Introduction & Objectives:**

Managing burn scars in children poses significant challenges in terms of treatment efficacy and safety. This study investigates various procedural methods for treating burn scars in children, focusing on their effectiveness, safety, standard protocols, and tolerability.

# **Materials & Methods:**

A comprehensive literature search was conducted on major databases, including PubMed, Scopus, and Web of Science, up to August 2024. The search emphasized procedural treatments for burn scars in children. Key data collected comprised participant demographics, sample sizes, intervention methods, follow-up protocols, treatment effectiveness, and reported adverse events. A total of 256 children were included in the assessment.

# **Results:**

All procedural treatments evaluated yielded satisfactory outcomes. Among the various methods, trapeze-flap plasty and percutaneous collagen induction demonstrated improvements in all patients. In the laser treatment group, which included 161 children, the Vancouver Scar Scale (VSS) score reduction ranged from 55.55% to 76.31%. Outcomes were rated as good (24.61%) to excellent (60%). Laser treatments, administered with local anesthesia, were well tolerated by the children. Overall, the study found that diverse methods—including trapeze-flap plasty, percutaneous collagen induction, phototherapy, and fractional CO2 laser—exhibited a relatively good response and an acceptable safety profile.

# **Conclusion:**

Various procedural treatments, particularly light-based therapies and lasers, demonstrate effectiveness and safety for treating burn scars in children. These methods often eliminate the need for general anesthesia, making them a viable option for scar management in this age group. The findings highlight the potential for improving treatment protocols tailored to children's needs.

Evaluating the combination and comparison of ablative fractional lasers (CO2, Erbium-YAG) with pulsed dye laser (PDL) for treating hypertrophic scars: a systematic review

Alireza Jafarzadeh\*1, azadeh goodarzi1

<sup>1</sup>Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran , Tehran, Iran

# **Introduction & Objectives:**

The aim of this study is to compare pulsed dye laser (PDL) and ablative fractional lasers (CO2, Erbium-Yag) in the treatment of hypertrophic and keloidal scars in a systematic review.

#### **Materials & Methods:**

Databases including Web of Science, Science Direct, Google Scholar and PubMed were searched for clinical trials up to December 1, 2024; focusing on the role of ablative fractional lasers and pulsed dye lasers in treating hypertrophic and keloidal scars, using comprehensive keywords and search syntaxes. Key data extracted included type of scars, the assessment indexes, treatment modalities, side effects and the final conclusion of each article.

# **Results:**

We\*\* didn't\*\* found any significant difference between the PDL and ablative fractional laser in the treatment of hypertrophic and keloidal scars, and both showed significant improvement. The average number of treatment sessions in the group receiving ablative fractional laser was 3.43 sessions, in the group receiving PDL, 3.68 sessions, and in the group receiving the combination of the two lasers, 1.5 sessions. Ablative fractional laser was 57.5% effective in VSS scoring and 40.4% effective in POSAS scoring, while PDL laser was 49.4% effective in VSS scoring and 35.5% effective in POSAS scoring , also the combination of both methods may lead to better results and higher efficacy with no severe adverse reactions noted.

#### **Conclusion:**

Ablative fractional laser and PDL are both effective in treating hypertrophic and keloid scars and there was no significant difference between them. Although, Studies investigating the combination of these two lasers have reported greater effectiveness than each method alone.

# Post-surgical Pyoderma Gangrenosum Following Mammoplasty: A Report of Two Cases

mustafa ürün<sup>1</sup>, Elif Bal Avcı<sup>1</sup>, Asena Kaşoğlu\*<sup>1</sup>

<sup>1</sup>trakya university, faculty of medicine, EDİRNE, Türkiye

# **Introduction & Objectives:**

Pyoderma gangrenosum (PG) is an uncommon inflammatory and ulcerative skin disorder, characterised histopathologically by the accumulation of neutrophils in the skin.Postsurgical PG (PSPG) is defined as the development of PG at the surgical site and typically develops within an average of 7 days after surgery. The condition is commonly diagnosed as a wound infection at presentation; nevertheless, treatment with antibiotics and wound debridement does not prevent the ulcer from progressing rapidly. The initial symptoms include surgical-site erythema and extreme pain. The majority of PSPG cases occurr~~ after breast surgery, particularly reduction mammoplasty procedures. Interestingly, over 50% of these cases involv bilateral breast procedures, resulting in bilateral PG.

#### **Materials & Methods:**

This report presents two cases of PG following bilateral reduction mammoplasty.

# **Results:**

# Case #1

A 63-year-old female patient was admitted to the plastic surgery department (PRS) on day 6 after bilateral reduction mammoplasty for IV antibiotic initiation due to redness and discharge at the wound site, initially suspected to be a wound infection. After 5 days of systemic antibiotic treatment with no clinical improvement, the patient was referred to the dermatology department. Dermatological examination revealed inverted T-shaped reduction mammoplasty scars in the bilateral periareolar areas, with ulcers measuring 10×10 cm and irregular, sharply demarcated necrotic tissue at the lower border of the scars, while the areolar areas remained intact. The patient was diagnosed with PG based on clinical and histopathological evaluation, and was admitted to the dermatology inpatient department for IV steroids and wound care. The patient's ulcers completely healed within six months following the addition of topical tacrolimus and the stepwise reduction of systemic corticosteroids, initially prescribed at 60 mg.

#### Case #2

A 24-year-old female patient was referred to the dermatology department from PRS on the fifth day after bilateral reduction mammoplasty due to fever and wound discharge. Dermatological examination revealed two annular ulcers measuring 3x3 cm, covered with granulation tissue, on the inferior bilateral areolae, and two necrotic ulcers measuring 5x5 cm in proximity to these, with preservation of the areolar area. Tissue and bacterial cultures were obtained and the results were negative. The patient was diagnosed with PG based on clinical and histopathologic evaluation. Following treatment with oral steroids, topical antibiotics, and tacrolimus, near-complete epithelialization of the ulcers was observed. Furthermore, a second surgical procedure was performed at the patient's request to facilitate wound closure. The ulcers healed almost completely after 3 months.

# **Conclusion:**

Postoperative PG is an exclusion diagnosis and should be considered when surgical wounds fail to respond to postoperative antibiotics. Initial treatment includes systemic steroids and wound care. Other immunosuppressive agents, such as cyclosporine or infliximab, may be used in refractory cases. Although surgical reconstruction is generally not recommended due to the risk of pathergy, it may be beneficial in some cases. No consensus currently exists on the diagnosis and treatment of PSPG, and prospective randomized controlled trials are needed.

# **Topical Timolol for the Healing of Complex Ulcers**

LEILA BENAHMED<sup>1</sup>, Nada Tahri<sup>1</sup>, kaoutar Belharti<sup>1</sup>, Nassiba Zerrouki<sup>1, 2</sup>, Nada Zizi<sup>1, 2</sup>

<sup>1</sup>Mohammed VI University Hospital Center, Dermatology, Venereology, and Allergology Department, Mohammed VI University Hospital Center, Oujda, Oujda, Morocco

<sup>2</sup>Mohamed I University, Epidemiology, Clinical Research, and Public Health Laboratory, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco, Oujda, Morocco

**Introduction & Objectives:** Chronic skin ulcers of microvascular origin, such as necrotic angiodermatitis and calciphylaxis, are severe dermatological conditions associated with significant pain, risk of infection, and functional impairment. These ulcers are particularly challenging due to the complex interplay of vascular compromise, systemic comorbidities, and limited therapeutic options. While conventional wound care and systemic management remain essential, new therapeutic approaches are being explored. Topical timolol, a non-selective beta-blocker with demonstrated effects on angiogenesis and tissue repair, has emerged as a potential adjunct in difficult-to-treat ulcers. This study reports four clinical cases illustrating the efficacy and safety of topical timolol in chronic ulcers of microvascular origin.

**Materials & Methods:** Four female patients, aged 57 to 74 years, were followed in the Dermatology Department of Mohammed VI University Hospital in Oujda, Morocco, for chronic lower limb ulcers of vascular origin. Diagnosis was based on clinical features, laboratory workup, vascular imaging (Doppler ultrasound, CT angiography), and histological examination. Common comorbidities included diabetes, end-stage renal disease, systemic sclerosis, and hypertension. After optimizing systemic disease management and initiating standard wound care, topical treatment with 0.5% timolol ophthalmic solution was introduced (1 drop per 2 cm², applied twice daily). Clinical follow-up focused on wound healing progression, pain improvement, and overall tolerance.

# **Results:**

- Case 1: A 57-year-old diabetic woman presented with painful ulcers of the legs and feet evolving over 4 months. Histology confirmed necrotic angiodermatitis. Topical timolol led to progressive healing and significant pain reduction within 3 months.
- Case 2: A 59-year-old woman with systemic sclerosis and refractory ulcers despite vascular management. Histology revealed dermal necrosis and microthrombosis. Timolol use resulted in marked pain relief after 1 month and substantial wound reduction by 4 months.
- Case 3: A 70-year-old woman with diabetes, hypertension, and ESRD on dialysis had necrotic ulcers with radiologic and histological evidence of calciphylaxis. Combined care with timolol facilitated wound healing over 4 months.
- Case 4: A 74-year-old woman with uncontrolled diabetes, dyslipidemia, and ESRD initially refusing dialysis presented with multiple necrotic ulcers. Histology confirmed calciphylaxis. After initiation of timolol and acceptance of dialysis, lesions showed progressive improvement and partial healing over 5 months.

**Conclusion:** Topical timolol proved to be a valuable therapeutic adjunct in chronic microvascular ulcers, promoting wound healing and pain control, even in patients with severe systemic comorbidities. Its ease of application, excellent local tolerance, affordability, and minimal systemic absorption make it particularly suitable in fragile populations. This case series highlights the potential role of timolol in managing complex ulcers, justifying further investigation through larger, controlled clinical studies.

"Traditional Scar Remedies: Myths, Practices, and Patient Perceptions"

fatine soulami<sup>1</sup>, Ouiame El Jouari<sup>1</sup>, Salim Gallouj<sup>1</sup>

<sup>1</sup>University Hospital Center of Tangier, tangier, Morocco

# **Introduction & Objectives:**

Scarring is a frequent dermatological concern with both functional and aesthetic implications. In Morocco, where traditional medicine plays a culturally significant role, many individuals rely on natural remedies for scar treatment. Despite their widespread use, these traditional practices are rarely studied or compared to modern therapeutic approaches. This study aimed to assess public perceptions and usage of traditional scar treatments in Morocco, identify commonly held beliefs and myths, evaluate perceived effectiveness, and compare these treatments to modern dermatological solutions.

#### **Materials & Methods:**

We conducted a cross-sectional descriptive study based on a structured questionnaire distributed to 189 participants living in both urban and rural areas of Morocco. The survey included questions on demographics, attitudes toward scarring, awareness and use of traditional vs. modern treatments, perceived effectiveness, safety perceptions, and the prevalence of popular beliefs or myths. Responses were analyzed using descriptive statistics to identify patterns and trends in the population.

# Results:

The study included 189 respondents, with 54% being female. Participants ranged in age from 18 to 65 years, and 72% resided in urban areas. Overall, 65% of participants found scars to be aesthetically disturbing. Notably, 43% believed scars would fully disappear over time, indicating limited understanding of scar physiology. Traditional treatments were widely known (82%), with the most cited remedies being shea butter (67%), olive oil (59%), and aloe vera (52%). Sixty percent of respondents had used at least one traditional remedy, with shea butter being the most commonly applied. Regarding effectiveness, 45% believed these treatments were moderately helpful, while 30% noticed visible improvement (reduction in scar size or discoloration). However, 25% reported no benefit. Awareness of modern treatments was lower (40%), and only 32% had tried options such as topical creams, silicone gels, or laser therapy. Those who used modern methods generally perceived them as more effective than traditional ones. Misconceptions were prevalent: 48% believed in popular myths, such as avoiding water on healing scars or applying substances like honey and butter to prevent scarring. Additionally, 60% believed traditional remedies were safer due to their natural origin. When asked about treatment preferences, 51% favored traditional treatments, citing lower cost (65%) and natural ingredients (58%) as key reasons. However, 30% felt traditional remedies should complement, not replace, modern treatments.

# **Conclusion:**

Traditional scar treatments are widely recognized and commonly used in Morocco, particularly due to cultural beliefs and accessibility. Despite limited scientific validation, these remedies remain popular and are often perceived as effective and safe. The study also reveals persistent myths and a limited understanding of scar healing processes. Modern treatments, though better recognized for efficacy, are underused—often due to cost or limited awareness. These findings highlight the need for targeted public education to bridge the gap between traditional practices and evidence-based dermatological care, ultimately improving scar management outcomes.



The efficacy, satisfaction, and safety of carbon dioxide (CO2) fractional laser in combination with pulsed dye laser (PDL) versus each one alone in the treatment of hypertrophic burn scars: a single-blinded randomized controlled trial

Alireza Jafarzadeh\*<sup>1</sup>, azadeh goodarzi<sup>1</sup>

<sup>1</sup>Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran , Tehran, Iran

# **Introduction & Objectives:**

Minimally invasive laser-based methods have gained attention for improving burn scars. This study aimed to evaluate the efficacy of two laser techniques—pulsed dye laser (PDL) and ablative fractional CO2 laser (AFCL)—and their combination on hypertrophic and keloid scars.

#### **Materials & Methods:**

A randomized single-blinded clinical trial was conducted on patients with hypertrophic or keloid burn scars. Participants were randomly assigned to three groups: PDL alone, AFCL alone, or a combination of PDL and AFCL. Assessments were conducted before treatment and 40 days post-final session, utilizing the Vancouver Scar Scale (VSS) to measure improvements in scar characteristics, including color, vascularity, height, and pliability.

#### **Results:**

Significant improvements were observed in all groups based on the VSS scores, scar color, vascular bed, height, and pliability. Notably, the combination therapy group demonstrated the most pronounced improvements, particularly in vascularity and pliability. Although the differences between groups were not statistically significant, the combined treatment showed a high percentage of improvement in total VSS and its indicators. Variations in efficacy were noted between mature and immature scars; the combination treatment was particularly effective in enhancing pliability, vascularity, and color in the immature scar subgroup.

# **Conclusion:**

Combined treatment using PDL and AFCL may offer more significant improvements in the appearance and pathological characteristics of burn scars compared to each treatment alone, particularly for immature scars. The findings suggest potential clinical significance, highlighting the benefits of combination therapy in scar management.



A systematic review of the efficacy, safety and satisfaction of regenerative medicine treatments, including platelet-rich plasma, stromal vascular fraction and stem cell-conditioned medium for hypertrophic scars and keloids

Alireza Jafarzadeh\*<sup>1</sup>, azadeh goodarzi<sup>1</sup>

<sup>1</sup>Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran , Tehran, Iran

# **Introduction & Objectives:**

The primary objective of this study is to examine the efficacy of various regenerative medicine approaches—including platelet-rich plasma, cell therapy, stromal vascular fraction, exosomes, and stem cell-conditioned medium—in the healing of hypertrophic and keloid scars.

#### **Materials & Methods:**

A systematic search was conducted using major databases such as PubMed, Scopus, and Web of Science. Based on predefined inclusion and exclusion criteria, eight articles were selected for review. The selected studies comprised two non-randomized clinical trials (25%), one randomized single-blinded comparative study (12.5%), one retrospective clinical observational study (12.5%), and four randomized clinical trials (50%). Data extraction and analysis were carried out using EndNote X8 and Google Sheets to ensure systematic handling of relevant information.

# **Results:**

All eight studies demonstrated the effectiveness of regenerative medicine in treating hypertrophic scars and keloids. Among the studies, five (62.5%) focused on platelet-rich plasma, two (25%) examined stromal vascular fraction, and one (12.5%) explored stem cell-conditioned medium. In two studies (25%), regenerative therapies were adjunctive to standard treatments, while six studies (75%) evaluated these methods as monotherapy compared to standard care. Importantly, no serious side effects were reported among patients treated with these approaches.

# **Conclusion:**

Regenerative medicine appears to be an effective treatment option with minimal side effects for hypertrophic scars and keloids, applicable as either monotherapy or in combination with standard treatments. However, further research is warranted to comprehensively evaluate the effectiveness of all subcategories within this field.

# Plasma Rich in Growth Factors (PRGF) for the Management of Second Intention Closure Healing in Hidradenitis Suppurativa: A Prospective Study in Clinical Practice

Alexandra Alturo-Pons\*1, Rosa Maria Segura1, Maria Urbano-Alcaraz1, Eva Vilarrasa1

<sup>1</sup>Hospital de la Santa Creu i Sant Pau, Dermatology, Barcelona, Spain

# **Introduction & Objectives:**

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease characterized by painful abscesses, nodules, and tunnels, often requiring surgical intervention. Second intention healing, a common postoperative approach, is associated with prolonged healing times and complications, impacting patient quality of life.

Plasma rich in growth factors (PRGF) offers an innovative solution by delivering growth factors directly to wounds, promoting tissue regeneration, angiogenesis, and reduced inflammation. This study evaluates PRGF's efficacy in HS surgical management compared to standard care.

## **Materials & Methods:**

This prospective study has included 38 patients so far (20 lesions treated with PRGF, and 21 controls) undergoing surgical intervention for HS.

PRGF was prepared using the Endoret® (BTI) system: blood was centrifuged at 1300 rpm for 8 minutes to isolate the growth factor-rich fibrin biomaterial fraction, which was applied covering the resulting defect, immediately after the removal of the target lesion. This method aims to accelerate epithelialization by enhancing collagen synthesis and modulating inflammation.

Patient demographics, baseline HS severity, type, metrics, and location of lesion excised, surgical procedure performed, surgical defect volumes, re-epithelialization times, and complications were recorded. Controls received standard postoperative care.

#### **Results:**

The PRGF and control groups were comparable in demographic and clinical features (mean age: PRGF 44,9  $\pm$  12.5 years; controls 47  $\pm$  11.9 years; mean BMI: 28.11  $\pm$  5.32 kg/m<sup>2</sup>). Smoking prevalence was 75%. Baseline stable systemic therapies included antibiotics (10%), adalimumab (25%), and secukinumab (17%).

All lesions were dermal or dermo-hypodermal tunnels removed following deroofing (65%) or Skin-Tissue-sparing Excision with Electrosurgical Peeling (STEEP) technique (35%). The excised tunnels were mainly located in the axilla (33%), inguinal fold (25%) and gluteal regions (25%). Mean lesion dimensions and surgical defect volumes were similar across groups ( $8.5 \pm 4.1 \text{ cm}^3$ ).

PRGF-treated wounds healed significantly faster (mean re-epithelialization time:  $12.8 \pm 7.5$  days) compared to controls ( $21.2 \pm 9.1$  days; p < 0.05). PRGF application enhanced granulation tissue formation and wound closure.

Complications were fewer in the PRGF group (8%) than in controls (25%), including minor infections, delayed healing and pain (p < 0.05), whereas immediate post-operative bleeding was similar in both groups (2 patients, 16.6%). The recurrence rate of HS in the operated lesions was very low in both groups (1 patient in the control group, 8.3%), median follow-up time of 13 (IQR 1-21) months.

# **Conclusion:**

PRGF significantly accelerates wound healing and reduces complications in second intention closure for HS surgical defects. These findings support PRGF as a valuable adjunctive therapy, warranting further validation in larger studies or controlled trials.

Evaluation of the efficacy, safety and satisfaction rates of platelet-rich plasma, non-cross-linked hyaluronic acid and the combination of platelet-rich plasma and non-cross-linked hyaluronic acid in patients with burn scars treated with fractional CO2 laser: A randomized controlled clinical trial

Alireza Jafarzadeh\*1

<sup>1</sup>Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran , Tehran, Iran

# **Introduction & Objectives:**

Skin scarring from burns, injuries, stretch marks, and acne can lead to cosmetic and functional issues. Various treatments are available, including lasers, corticosteroid injections, surgery, and regenerative techniques such as platelet-rich plasma (PRP) and hyaluronic acid products. This study aims to evaluate the effectiveness of PRP, non-cross-linked hyaluronic acid, and their combination in improving burn scars, as well as their impact on quality of life and potential disabilities.

# Materials & Methods:

A clinical trial was conducted with 10 individuals suffering from burn scars between 2023 and 2024. Participants underwent CO2 fractional laser treatment followed by injections of PRP, non-cross-linked hyaluronic acid, or a placebo in the scar areas. The treatment was performed over two sessions with a one-month interval. Evaluations included the Vancouver Scar Scale (VSS), biometric assessments (tewametry, corneometry, erythema index, melanin index, cutometry, thickness, and density), ultrasounds, and satisfaction ratings. Assessments were conducted at baseline, one month post-first session, and three months post-first session.

## **Results:**

Significant improvements in biometric parameters were observed in the intervention groups compared to the placebo group (p < 0.05). Both PRP and non-cross-linked hyaluronic acid treatments, as well as their combination, demonstrated the best clinical responses, with significant differences noted among groups (p < 0.05). Dermal thickness did not show significant improvement across treatment sessions, and variations among subjects were not significantly different. Colorimetry significantly improved in all groups except the placebo group, with no notable differences between intervention groups. The VSS significantly decreased in all treatment groups compared to the placebo.

## **Conclusion:**

PRP, non-cross-linked hyaluronic acid, and especially their combination are effective treatments for burn scars, demonstrating significant improvements in clinical outcomes and patient satisfaction. These findings support the use of these treatments in clinical practice to enhance scar appearance and potentially improve quality of life for affected individuals.

# Heterotopic Ossification Secondary to Chronic Venous Insufficiency A Case Report

Raluca Ioana Ailincăi\*<sup>1</sup>, Silviu-Horia Morariu<sup>1</sup>

<sup>1</sup>Mures County Clinical Hospital, Dermatology , Targu Mures, Romania

# **Introduction & Objectives:**

Heterotopic ossification secondary to chronic venous insufficiency is a rare condition characterized by the formation of mature bone within soft tissues.

#### **Materials & Methods:**

We report the case of a 67-year-old female with a long-standing history of stage VI chronic venous insufficiency and multiple comorbidities, including arterial hypertension, diabetes mellitus, and chronic kidney disease. Dermatological examination revealed a circumferential ulcer on the right leg, measuring approximately 19 × 26 cm and 1 cm in depth, covered with fibrin deposits and yellow-green exudate, with sharply demarcated erythematous margins. In the proximal third of the ulcer, a 15 mm erythematous nodular mass was noted, surrounded by white, hard, calcified-appearing fragments. The fragments were extracted and histopathologically analyzed. The ESR was high. Other laboratory tests, including serum calcium, parathyroid hormone, and alkaline phosphatase levels, were within normal limits. *Pseudomonas aeruginosa, Staphylococcus aureus*, and *betahemolytic Streptococcus were isolated from the wound*. Plain radiographs of the right leg revealed multiple well-defined radiopaque masses, diffusely spread in the soft tissue. Histopathological exam confirmed the diagnosis of osteoma cutis.

**Results:** \*\* Extensive surgical debridement was not feasible due to the widespread distribution of the osteoma cutis. Therefore, a conservative management approach was chosen. The patient received a 7-day course of colistin (6 million units/day) and ceftriaxone (4 g/day) systemic therapy. Locally, wet dressings with boric acid and silver sulfadiazine ointment were recommended. No complications have occured during the follow-up period.

# Conclusion:

There are no established treatment guidelines for heterotopic ossification secondary to chronic venous insufficiency. This case shows a rare presentation of heterotopic ossification, emphasizing the importance of effective preventive strategies in patients with venous leg ulcers.

# Effect of Topical Timolol on Healing of Immature Breast Scars After Mammoplasty: A Randomized Controlled Trial with Blinded Assessors and Patients

Alireza Jafarzadeh\*1

<sup>1</sup>Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran, Tehran, Iran

# **Introduction & Objectives:**

Wound healing is a complex process encompassing four main stages: hemostasis, inflammation, cell proliferation, maturation, and differentiation. Timolol (TM) may influence these stages, particularly re-epithelialization. This study aims to evaluate the one-month effects of timolol on acute surgical wounds in post-mammoplasty patients. to investigate the efficacy of topical timolol in improving postoperative breast scars, aiming to guide future treatment protocols and prescriptions.

## **Materials & Methods:**

A total of 12 patients who underwent bilateral mammoplasty were enrolled in this double-blind randomized clinical trial. Treatment commenced 48 hours post-surgery; one breast was treated with 0.5% timolol eye drops, while the contralateral breast received distilled water (control). Patients were advised to minimize sun exposure and pressure on the treated area, with no additional oral or topical medications prescribed. Cleansing with a prescribed cleanser occurred every three days. Cosmetic assessments were conducted by a specialist at 10 and 30 days post-surgery using a 10-point Likert scale. Data were analyzed using Two-Way Repeated Measures ANOVA.

#### **Results:**

Timolol significantly reduced erythema over time (Interaction, P<0.0001; Treatment, P=0.02), with an average decrease of 5.38 points (CI95%: 4.22-6.55) compared to 4.41 points (CI95%: 3.83-5) for placebo. The difference in reduction was 0.972 points (CI95%: 0.18-1.7). A significant improvement in the aesthetic appearance of the breast was also noted (Interaction, P<0.0001; Treatment, P=0.015), with timolol enhancing the aesthetic score by approximately 5.5 points (CI95%: 4.9-6.2) versus 4.58 points (CI95%: 3.4-5.7) for the placebo. Overall, timolol improved the aesthetic score by 0.972 points (CI95%: 0.23-1.7) more than the placebo.

# **Conclusion:**

Topical application of 0.5% timolol for at least one month positively affects the aesthetic quality of breast scars following mammoplasty, as well as reducing erythema and inflammation in the wound area

# Perforating Granuloma Annulare: an interesting case of a rare variant

Themis Sgontzou<sup>1</sup>, Margarita Gerolympou<sup>1</sup>, Melpomeni Theofili<sup>1</sup>, Alexander Stratigos<sup>1</sup>, Eftychia Zouridaki<sup>1</sup>

<sup>1</sup>Andreas Sygros Hospital of Venereal and Skin Disease, 1st Department of Dermatology-Venereology, Medical School, National and Kapodistrian University of Athens, Athens, Greece

# **Introduction & Objectives:**

Perforating granuloma annulare (PGA) is a rare variant of granuloma annulare (GA), a benign, self-limited dermatosis marked by necrobiotic granulomas. Clinically, PGA presents as umbilicated papules or pustules, primarily on the extremities, often with central crusting or ulceration. It can mimic conditions like cutaneous sarcoidosis, necrobiosis lipoidica, papulonecrotic tuberculid, reactive perforating collagenosis, and psoriasis. Dermoscopy shows central whitish to yellowish-orange or brown structureless areas, radial dotted and linear vessels, peripheral dam-shaped elevation, and a white irregular halo with a thin scale ring. Treatment includes topical corticosteroids, phototherapy, and systemic therapies, with recent studies highlighting the potential benefit of biologics like adalimumab. We report this case to emphasize the need to consider PGA in ulcerated lesions with atypical features.

# **Materials & Methods:**

A 69-year-old Caucasian female with a medical history of diabetes mellitus type II and hypercholesterolemia under treatment with insulin analogs, dapaglifozin, and statins respectively, presented to the outpatient department with mildly pruritic annular erythematous plaques with peripheral scaling on both upper and lower extremities, persisting for approximately 3 months. Certain lesions exhibited areas of ulceration within the primary plaques, for which she was referred to the Ulcer Day Hospital Unit. A skin biopsy was performed\*\* and the ulcers were managed with standard care for wound healing while waiting for the result.

# **Results:**

Taking into consideration the clinical presentation which included the presence of erosions and ulcers and the histological findings the diagnosis of PGA was made. The patient was administered acitretin 25 mg daily, with a good therapeutic response and the lesions resolved after 2 months of treatment with no evidence of recurrence to date.

#### **Conclusion:**

PGA remains a rare and often treatment-resistant variant of GA. A definitive diagnosis requires skin biopsy and histopathological analysis, which reveals trans-epidermal elimination of necrobiotic collagen. Its etiology remains unclear but may be associated with systemic conditions such as diabetes mellitus, a comorbidity present in our patient. Reccurence is not uncommon especially, in its generalized or disseminated forms. Despite being regarded as resistant to therapy, in this case systemic acitretin led to the complete resolution of lesions. Early recognition and appropriate treatment are essential to achieve sustained remission. Therefore, studies are needed to establish standardized therapeutic approaches for this uncommon variant.

# Trichloroacetic Acid as a Chemical Debridement Agent in Wound Healing

Inas Chikhaoui<sup>1</sup>, Madiha El Jazouly<sup>1</sup>, Sara Nejjari<sup>1</sup>, Ghita Basri<sup>1</sup>, Soumia Chiheb<sup>1</sup>

<sup>1</sup>Cheikh Khalifa Bin Zayed Al Nahyan Hospital, Casablanca

# **Introduction & Objectives:**

Chronic wounds, characterized by fibrin, devitalized tissues, and bacterial debris, often lead to refractory ulcers. Trichloroacetic acid (TCA), widely used for dermatological conditions such as warts and acne scars, has emerged as a promising chemical debridement agent. This study evaluated TCA's efficacy in promoting wound healing by removing necrotic tissue while preserving viable tissue, enhancing growth factor expression and epidermal renovation, and comparing its advantages over mechanical debridement.

## **Materials & Methods:**

The protocol involved weekly application of 50% TCA via cotton swab to devitalized tissue until frosting appeared, followed by wound dressing. Patients with various wound types, including chronic vascular ulcers, pressure ulcers, livedoid vasculopathy, and diabetic abscesses, were included. Clinical outcomes were assessed through pre- and post-treatment photographs and healing progression. TCA works through protein denaturation, exhibiting selective toxicity to keratinocytes and fibroblasts while reducing metalloproteinases. Its hemostatic properties minimize bleeding during debridement, and it upregulates growth factors such as TGF- $\beta$  to accelerate remodeling.

## **Results:**

The study demonstrated that TCA achieved rapid debridement, reduced healing time, and improved tissue granulation across diverse wound types, including prolidase deficiency ulcers and perforating plantar disease. Key advantages of TCA include its selectivity in preserving healthy tissue compared to mechanical methods, simplicity of application, painless procedure, cost-effectiveness, and absence of adverse effects. While TCA is well-established in cosmetic procedures, this study highlights its therapeutic potential in complex wounds, aligning with existing literature on its role in MMP downregulation and growth factor stimulation.

# **Conclusion:**

In conclusion, TCA chemical debridement is a safe, effective, and accessible option for chronic wound management, offering significant clinical and economic benefits. Further randomized trials are recommended to standardize protocols and confirm these findings.

# Innovative Wound Care Approach in a Complex Case Involving Osteomyelitis: First Use of Vacuum Therapy in a Clinical Setting

Greta Szemethy<sup>1, 1</sup>, Lilla Tóthné<sup>1</sup>, Zoltánné Szabó<sup>1</sup>, Viktória Köröczné<sup>1</sup>

<sup>1</sup>Veszprém Vármegyei Csolnoky Ferenc Kórház, Bőrgyógyászat, Veszprém

# **Introduction & Objectives:**

Managing chronic, hard-to-heal wounds presents a significant clinical challenge, especially in polymorbid patients. This report describes the first application of negative pressure wound therapy (NPWT) in our clinical setting, used to treat a male patient with a severe heel ulcer complicated by osteomyelitis. The outcome highlights the potential of NPWT in similarly complex cases.

#### **Materials & Methods:**

The patient was a 60-year-old male with insulin-dependent diabetes mellitus, hypertension, diabetic nephropathy requiring long-term hemodialysis, peripheral neuropathy, and visual impairment. He had a history of Lisfranc amputation due to recurrent osteomyelitis and developed permanent lower limb paraparesis after an epidural abscess, resulting in a bedridden state.

He presented with a chronic, non-healing heel ulcer complicated by osteomyelitis. Emergency surgical debridement was performed, followed by the initiation of NPWT and systemic antibiotics. Treatment continued with daily wound monitoring, infection control, and supportive care.

## **Results:**

During the first 14 days, the wound was surgically debrided, and NPWT initiated. Healing tendencies allowed transfer to a dermatology-focused care setting, where NPWT and parenteral antibiotics continued. MRSA was identified in cultures, allowing targeted antimicrobial therapy. Over the next 52 days, the wound showed reduced inflammation, peripheral epithelialization, and decreased exudate. After discharge, outpatient follow-up maintained progress.

Upon readmission on day 155, granulation tissue fully covered the wound base, with no recurrence of sepsis or need for amputation. Continued outpatient management with oral antibiotics and home dressings led to further improvement.

# **Conclusion:**

NPWT proved highly effective in promoting wound healing and preventing limb amputation in a polymorbid patient with a complex, infected pressure ulcer. This method offers significant therapeutic potential where traditional surgical interventions are not feasible or are declined by the patient. NPWT can serve as a valuable limb-salvage option in similarly critical wound care cases.

# Tolerance and Efficacy of a Massage Gel in Adults and Adolescents with recent and Red Scars

Armony Philippe<sup>1</sup>, Marie-Dominique Thouvenin<sup>1</sup>, Gautier Doat<sup>2</sup>, Aline STENNEVIN\*<sup>2</sup>

<sup>1</sup>Pierre Fabre Dermo-Cosmetics & Personal Care, R&D Department, Toulouse, France

# **Introduction & Objectives:**

Achieving high-quality scar healing is a key expectation for patients. Scar massage with an appropriate product is often recommended by surgeons or dermatologists to enhance aesthetic outcomes.

The objective of this study was to evaluate the tolerance and efficacy of a new massage gel containing a bacterial extract called *Aquaphilus dolomiae*, dimethicone, and hyaluronic acid.

#### **Materials & Methods:**

Fifty-four subjects (adolescents and adults from 12 to 64 years) with re-epithelialized recent and red scars (post-surgical and post-suturing traumatic scars) located on the face, body, or scalp were included in an open-label clinical study. The product was applied twice daily on the re-epithelialized immature and red scar for 85 days, following a standardized massage protocol. The visits were performed at Day 1, Day 22, Day 57 and Day 85. The primary objective was to assess product tolerance by a dermatologist. Secondary objectives included clinical efficacy evaluated using the Patient and Observer Scar Assessment Scale (POSAS), the intensity of discomfort assessed with an 11-point numerical rating scale (NRS), erythema evolution measured using a spectrophotometer, a cosmetic acceptability questionnaire, and standardized photographs.

# Results:

The cutaneous tolerance was assess as very good by the investigator.

A significant improvement in the POSAS score was observed by both the investigator and the subjects: -27% and -37% at Day 22, -47% and -54% at Day 57, and -65% at Day 85 (p<0.0001), respectively.

A statictically significant improvement of all sub-parameters of POSAS assessed by the Investigator (pigmentation, pliability, relief, surface, thickness and vascularity) were also observed from D22 until D85 (p<0.0001).

Subjects also reported a soothing effect, characterized by a significant reduction in discomfort: -38% at Day 22, -59% at Day 57, and -77% at Day 85. Erythema improvement was observed through spectrophotometric measurements, showing a significant increase in parameter L\* and a decrease in parameter a\* at each follow-up visit. The product's cosmetic qualities were well appreciated by the subjects.

#### **Conclusion:**

The tolerance and efficacy results of this study suggest that this massage gel may be beneficial in improving the aesthetic outcomes of immature scars in both adults and adolescents conducting to an improvement of the patients' quelity of life.

<sup>&</sup>lt;sup>2</sup>Pierre Fabre Dermo-Cosmetics & Personal Care, Laboratoire Dermatologique Eau Thermale Avène, Lavaur, France



Effectiveness and tolerance of an extract-based scar gel of Aquaphilus dolomiae, dimethicone, hyaluronic acid combined with a massage method on re-skinned post-burn and post-surgical scars: 6-month follow-up

Nicolas Frasson<sup>1</sup>, Marine Babin<sup>2</sup>, Adeline Bacquey<sup>2</sup>, Gautier Doat<sup>3</sup>, Aline STENNEVIN\*<sup>3</sup>, Therese Nocera<sup>2</sup>

# **Introduction & Objectives:**

Wound healing is a complex process which aims to restore the physiological

function of the skin barrier and ensure skin comfort. For optimal hydration, hyaluronic acid (HA) is preferred, while silicone-based topical silicone-based topical products improve the skin's softness and elasticity, particularly in the post-burn phase. This study evaluates the benefit and tolerability of a gel containing Aquaphilus dolomiae, dimethicone, HA combined with an educational program using a validated massage method, on post-burn scars and surgical scars.

## **Materials & Methods:**

A population of adults and children (aged 2 to 65) was included in the study, which was conducted in the spirit of good clinical practice. 4 follow-up visits: Tbaseline, T3, T12 and T24 weeks. The product was applied 2/day to reepidermized post-surgical and post-burn scars ( $\leq$ 10% of BSA in children;  $\leq$ 30% in adults).

Assessments at each visit: Patient and Observer Scar Assessment Scale (POSAS 2.0); Investigator Global Assessment relating to scar appearance (IGA score in 5 grades); vitro-pressure skin test; instrumental assessment of erythema by chromametry; overall tolerance and product satisfaction (investigator and subject).

## **Results:**

35 subjects included, 11% of whom were children, 18 cases of post-burn limb scars and

17 post-surgical. The results confirm the improvement in clinical and instrumental scar assessment scores from T3 weeks: significant decrease (S) (p<0.05) in investigator and subject POSAS scores; improvement in IGA with approximately 74.2% of subjects showing "clear" or "very clear improvement" at T3 weeks; 81.8% and 100% at T12 and T24 weeks. Clear improvement (S) in "itching" (particularly post-burn) and scar "pain" scores (POSAS subject) of -32%\* and -43%\* respectively from T3. The evolutionary aspect of the scar assessed by the expert investigator was judged to be "very satisfactory" in around 77% of cases from 3 weeks and up to 100% at the end of the study. Clinical improvement was associated with a significant reduction in the severity of erythema (p<0.05) measured by chromametry (parameter a\*) as early as 3 weeks and was optimised up to T24 weeks (p<0.001). Tolerance of the product was assessed as "excellent" throughout the study. Subjects were 95% satisfied with the product from T3 and 100% at the end of the study.

## **Conclusion:**

This clinical and instrumental study with 6-month follow-up suggests the benefit and excellent tolerance of the scar gel combined with the massage technique in the aftermath of scarring post-burns and post-surgery in the

<sup>&</sup>lt;sup>1</sup>Clinique STER, Lamalou-les-bains, France

<sup>&</sup>lt;sup>2</sup>Pierre Fabre Dermo-Cosmetics & Personal Care, R&D Department, Toulouse, France

<sup>&</sup>lt;sup>3</sup>Pierre Fabre Dermo-Cosmetics & Personal Care, Laboratoire Dermatologique Eau Thermale Avène, Lavaur, France

short and medium term.

The dermocosmetic product improves the softness and skin elasticity too.



Successful Management of a Chronic Leg Ulcer Using Methylene Blue Daylight Photodynamic Therapy and Split-Thickness Skin Graft

Ahmet Ataş<sup>1</sup>, Erhan Topal<sup>1</sup>, Mustafa Andıç<sup>1</sup>, Kıymet Nur İskender<sup>1</sup>, Demet Sezen<sup>1</sup>, Vildan Çakır Köse<sup>1</sup>, Tülin Ergun<sup>1</sup>, Dilek Seçkin<sup>1</sup>

<sup>1</sup>Marmara University School of Medicine, Department of Dermatology, Istanbul, Türkiye

**Introduction & Objectives:** Chronic leg ulcers, which result in the loss of full-thickness skin tissue, are challenging conditions for dermatologists, particularly when venous insufficiency is the underlying etiological factor. The treatment generally involves a combination of addressing the underlying cause, wound care dressings, and surgical interventions. Among the treatment options, photodynamic therapy and split-thickness skin grafts are less commonly used but potentially effective methods. We will discuss here a case of chronic venous leg ulcer successfully treated with a combination of photodynamic therapy and skin grafting

Materials & Methods: A 26-year-old male presented to our clinic with a unilateral leg ulcer that had been present for 3 years. Medical history revealed epilepsy and Burkitt's lymphoma which was in remission. Previous treatments included wound care, several courses of oral antibiotics, and PRP therapy. Doppler ultrasonography revealed significant venous reflux in both the great and small saphenous veins. On physical examination, there were two ulcerative lesions on the left pretibial area: one measuring 3.6x4.4 cm and the other 1.6x1.6 cm, featuring yellow-black crusts and bleeding areas. Due to the erythema and induration in the surrounding skin, differential diagnoses included lipodermatosclerosis-associated ulceration, pyoderma gangrenosum, and necrobiosis lipoidica. Histopathological evaluation confirmed a nonspecific granulation tissue response, and bacterial cultures revealed methicillin-sensitive Staphylococcus aureus. The patient underwent a course of systemic antibiotic therapy which resulted only in partial improvement. Daily photodynamic therapy was started by applying methylene blue solution with an occlusive dressing for 30 minutes, followed by daylight exposure. The ulcer was then covered by an antibacterial wound dressing and elastic bandage up to the knee. After 10 days, the ulcer had a clean base but remained in the same size and showed no sign of epithelialization. So, a split-thickness skin graft was harvested from the anterior thigh using a sterile technique. Multiple small grafts were applied to the ulcer and secured with sterile cigarette paper and elastic bandaging. During subsequent weekly follow-ups, the wound bed was cleaned and re dressed with an antibacterial dressing. At the end of the 11th week, complete epithelialization of the lesion was observed

**Results:** Involving the transfer of the epidermis and part of the dermis, split-thickness skin grafting requires a well-vascularized wound bed due to its lack of blood supply. It can be sourced from various donor types and anatomical sites.

**Conclusion:** In our case, combined use of photodynamic therapy and split-thickness grafting resulted in complete epithelialization of a chronic ulcer and high patient satisfaction. This method offers successful healing and patient comfort.

# A pediatric case of nevus comedonicus on grafted skin: Coincidence or pathogenic consequence?

Hind Majdoul<sup>1</sup>, Fatima Zahra El Fatoiki<sup>1</sup>, Hali Fouzia<sup>1</sup>, Soumiya Chiheb<sup>1</sup>

<sup>1</sup>Ibn Rochd University Hospital, Dermatology and Venereology Department, Casablanca

## **Introduction & Objectives:**

Comedonal hamartomas, or nevus comedonicus (NC), are rare epidermal malformations of the pilosebaceous unit, typically congenital or arising in childhood. In uncommon instances, NC may may develop de novo following skin trauma, burns, infections, or vaccinations—through Koebner or Wolf isotopic responses.

We report an extremely rare case of NC arising in a skin graft, further illustrating how localized skin injury can trigger hamartomatous proliferation.

#### **Materials & Methods:**

#### **Results:**

## Case presentation:

A 9-year-old girl with no significant past medical history who suffered a scald burn two years prior, for which she underwent split-thickness skin grafting, presented to our department one year after the graft, with grouped comedonal lesions localized to the graft site, predominantly along its periphery. Clinical examination revealed multiple open comedones arranged in a linear pattern at the edges of the graft, extending across the base of the neck, the lower chest, and the proximal upper limbs. The lesions appeared as dilated follicular openings filled with dark keratin plugs, resembling classic features of nevus comedonicus. Histopathological analysis confirmed the diagnosis of a comedonal hamartoma, showing dilated follicular infundibula filled with lamellar keratin. Treatment included mechanical extraction of comedones and topical retinoids, leading to partial cosmetic improvement. Follow-up showed lesion stability without new flare-ups or complications.

#### **Conclusion:**

Acquired nevus comedonicus (NC) on grafted or scarred skin is an exceptional entity, reflecting post-traumatic cutaneous mosaicism. Several cases have described NC arising weeks or months after localized skin injury, such as burns, herpes zoster, or deep infections. These lesions are typically asymptomatic, presenting as grouped open comedones over the affected area. Histologically, they feature dilated follicular structures packed with lamellar keratin, minimal inflammation, and no atypia—confirming their benign hamartomatous nature. The pathogenesis is thought to involve postzygotic somatic mutations unmasked by local disruption of the epidermal microenvironment. Koebner and Wolf isotopic responses are implicated, with the latter being most plausible in patients without a pre-existing NC. Management is usually conservative: mechanical comedone extraction and topical retinoids may improve appearance, while surgical excision or ablative options such as CO<sub>2</sub> laser treatments can be considered in persistent or cosmetically bothersome cases. Malignant transformation has not been reported, and most lesions remain stable or resolve spontaneously. In our case, we question whether the lesion represents a truly acquired NC induced by the graft environment, or rather a coincidental occurrence of NC during childhood in a grafted area. However, the precise distribution of lesions along the graft margins raises the possibility of a localized trigger, supporting a trauma-related origin rather than mere coincidence. Given the rarity of NC arising on grafted skin, each new case warrants thorough documentation to better understand its

pathophysiology and clinical implications.

# A Rare Presentation of Pyoderma Gangrenosum: Pathergy at Split-Skin Graft Donor Site

Shubhangi Gupta\*1, sanjeev gupta1

<sup>1</sup>dr. dy patil medical college, hospital and research centre, pimpri, dermatology, pune, India

# **Introduction & Objectives:**

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis in which papulopustules rapidly evolve into painful, necrotic ulcers with violaceous, undermined borders. Trauma-induced lesions ("pathergy") may arise at sites of venipuncture, surgery, or grafting. When PG appears at surgical or graft-donor sites within days of the procedure, it is termed post-surgical PG (PSPG). We describe a 25-year-old woman whose chronic lower-limb and hand ulcers—initially labeled non-healing and treated with skin grafting—worsened via pathergy. Our objectives were to (1) characterize this atypical post-graft PG, (2) outline a focused diagnostic and therapeutic strategy, and (3) underscore the importance of advanced wound dressing and clinical vigilance.

## **Materials & Methods:**

A previously healthy 25-year-old woman presented with bilateral lower-leg and right-hand ulcers persisting for two years. Lesions developed following COVID-19 vaccination and, after failing to heal, underwent split-skin grafting. Within days, a new ulcer appeared at the graft-donor site, indicating pathergy. There was no personal or family history of systemic disease. Skin biopsy revealed a dense neutrophilic infiltrate and dermal necrosis, consistent with PG. Laboratory evaluation showed hemoglobin 5.6 g/dL (two units of packed red blood cells transfused), with normal liver and renal panels, inflammatory markers, and negative autoimmune serology. Treatment comprised cyclosporine (5 mg/kg/day), oral prednisone (1 mg/kg/day), and topical colloidal silver dressings changed every 48 hours.

## **Results:**

Within four weeks of immunosuppression, ulcer expansion ceased and granulation tissue emerged. Colloidal silver maintained a moist, antimicrobial wound environment, yielding a 40 % reduction in ulcer area by eight weeks. At three months, 50 % of ulcer surfaces were re-epithelialized, pain had markedly improved, and no new pathergic lesions developed. Hemoglobin stabilized at 11 g/dL. Immunosuppressants were gradually tapered over six months, by which time 70 % of ulcer surfaces were re-epithelialized. No significant adverse effects from therapy or dressings occurred.

# **Conclusion:**

This case illustrates PG's propensity for pathergy at graft and donor sites, resulting in chronic, necrotic ulcers when unrecognized. Early identification of PG and avoidance of further surgical trauma are critical. Systemic cyclosporine combined with corticosteroids effectively controlled inflammation, while colloidal silver dressings provided antimicrobial protection and optimal moisture balance, accelerating healing. Clinicians should suspect PG in any non-healing ulcer—especially when pathergy is evident—and promptly institute immunosuppression alongside advanced wound care to reduce morbidity and improve outcomes.