Harnessing the Body's Natural Healing Power:

A Case-Based Approach To Autologous Multilayered Leukocyte, Platelet, and Fibrin Patches

Supported by an educational grant from Reapplix.

Faculty

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Faculty Disclosures

- **Tyson Green, DPM**
  Founder/Owner: Imperial Pointe Wound Center
  Advisor/Speaker: Reapplix
- **James Y. Lin, DO, MS (MedEd), MHSA**
  Nothing to disclose in relation to this activity
- **Anthony Tickner, DPM, FACCWS, FAPWH, FRCPS**
  Nothing to disclose in relation to this activity

Learning Objectives

- Review the science and clinical application of an autologous multilayered leukocyte, platelet, and fibrin (MLPF) patch and distinguish from other autologous blood-derived products
- Analyze results from a retrospective data analysis on healing outcomes of chronic, hard-to-heal diabetic foot ulcers (DFUs) treated with an autologous MLPF patch in a real-world clinical setting
- Examine the impact of an autologous multilayered patch composed of leukocytes, platelets, and fibrin on the perfusion of a chronic wound
- Examine the integration of an autologous MLPF patch into a clinic workflow
- Explore illustrative case studies using autologous MLPF patch on chronic wounds

DFU = diabetic foot ulcer.

Autologous Wound Treatment Option – 3C Patch: Science and Clinical Application

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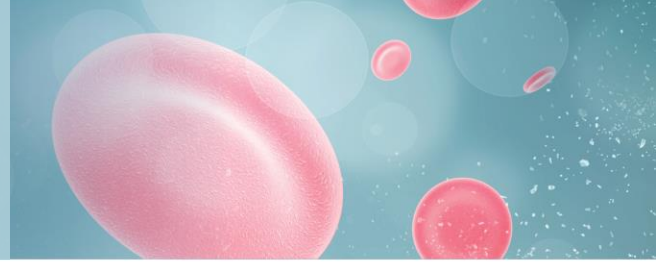
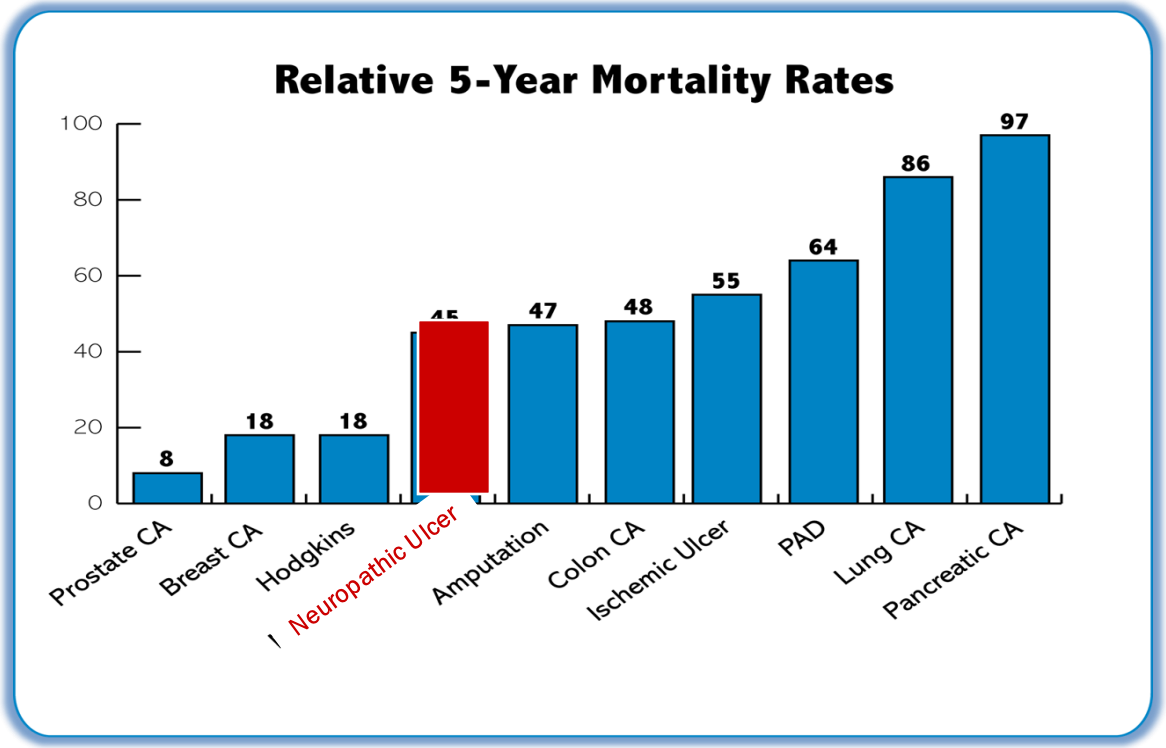
Agenda



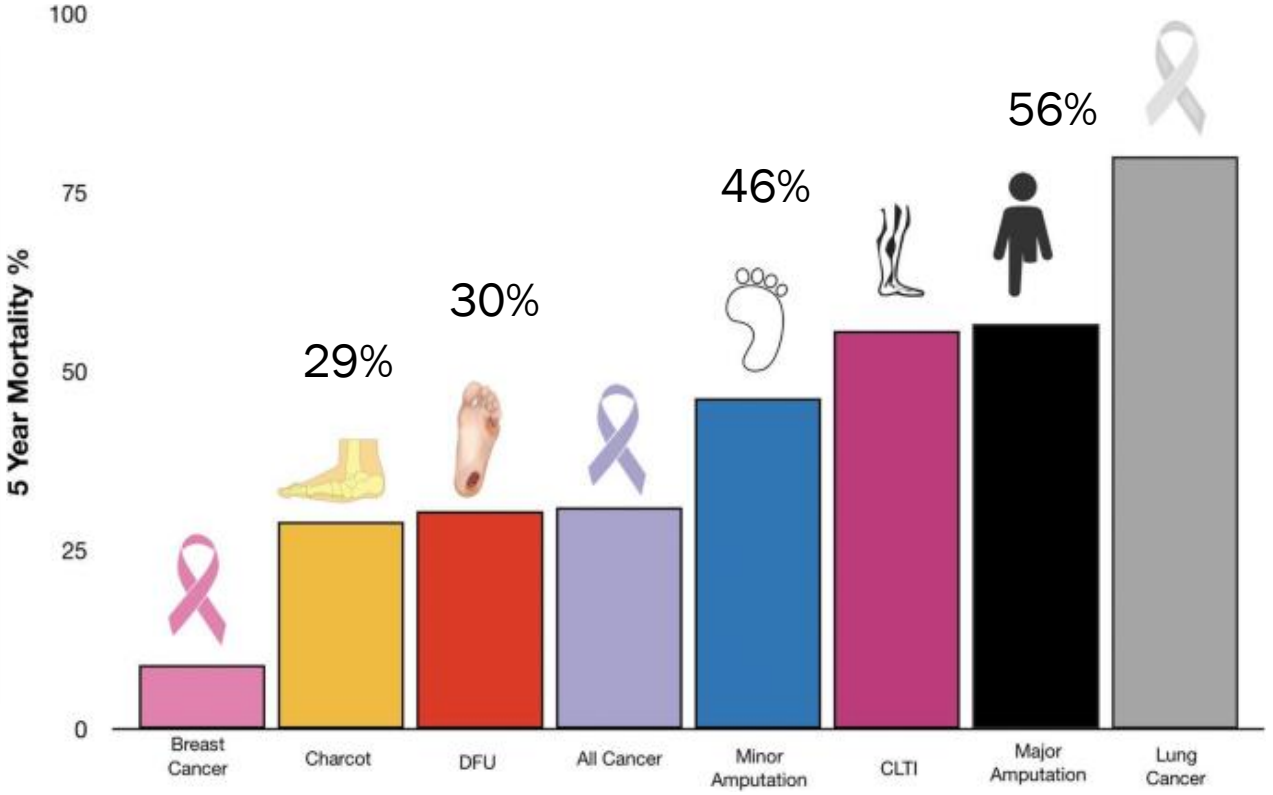
- Why efficient wound healing is important?
- What is 3C (autologous MLPF) Patch?
- Clinical information behind 3C Patch
- Use on larger wounds, over bone, over tendon
- Effective patient ID
- Patient outcomes

Consequences of Unhealed Neuropathic Ulcers

2007



2020



- Nearly half of all unhealed neuropathic ulcers result in death within 5 yrs

Armstrong, D.G., Swerdlow, M.A., Armstrong, A.A. *et al.* Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. *J Foot Ankle Res* **13**, 16 (2020). https://doi.org/10.1186/s13047-020-00383-2

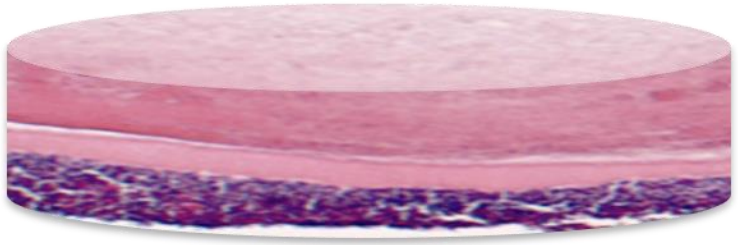
Armstrong DG. *Int Wound J*. 2007;4(4):286-287.

What Is an Autologous MLPF Patch?

3-layer autologous multilayered leukocyte, platelet and fibrin patch

Histological image highlighting the 3-layers of the patch

1
2
3



Actual image of the patch

The 100% autologous patch is produced at the point of care from the patient's own blood

1. Fibrin
2. Approximately 3 billion platelets
3. Approximately 50 million leukocytes

Clinical Effect of the 3-Layer Structure In Wound Healing

FIBRIN

Provides moisture retention and structural integrity, making handling and application easy.

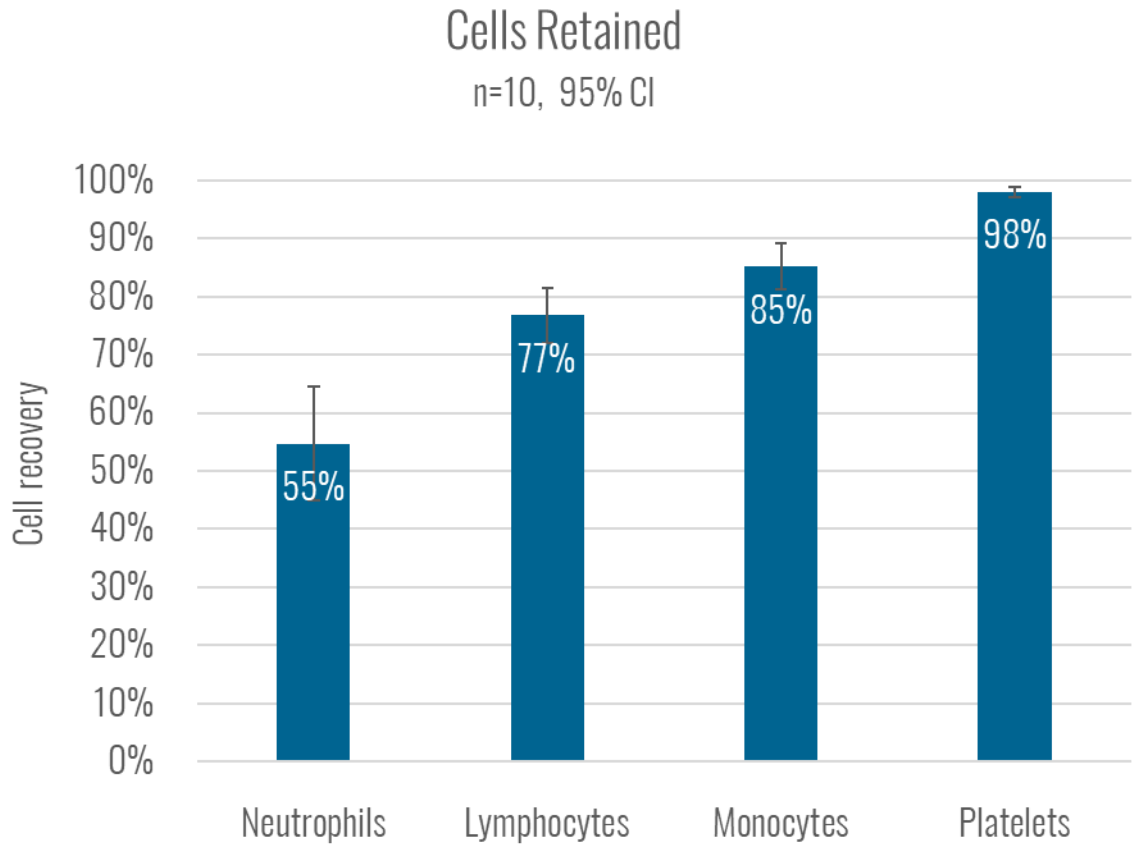
LEUKOCYTES

Approximately 50 million leukocytes, known to orchestrate healing and fight infection, are provided directly to the wound surface

PLATELETS

Approximately 3 billion platelets, known to provide high growth factor levels

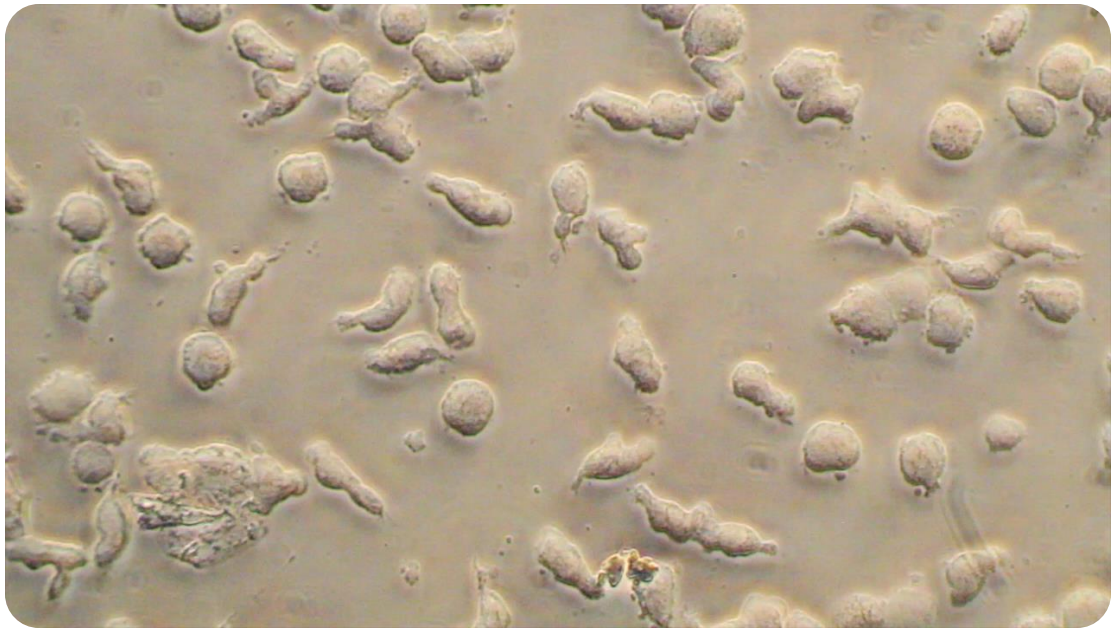
Recovery Rates of Cells and Platelets In the Autologous Patch



Lundquist et al (2013) *Wound Repair and Regeneration*

Role of Leukocytes in Wound Healing

- The leukocyte layer in autologous MLPF patch contains a high concentration of neutrophils, monocytes (pre-cursor to macrophages), and lymphocytes
- Neutrophils and macrophages are known to remove bacteria and debris from the wound bed
- Once bacteria and debris are removed, the macrophages as well as lymphocytes, are involved in the resolution of the inflammatory response and signal the wound to progress to healing
- In-vitro evidence shows that the cells in the autologous MLPF patch respond differently to different wound-related signals and are capable of releasing both pro- and anti-inflammatory cytokines
- The effect of the autologous MLPF patch on *Pseudomonas aeruginosa* bacteria was tested in simulated biofilms and showed a significant reduction of the bacterial culture, thus potentially limiting the development of biofilms in wounds

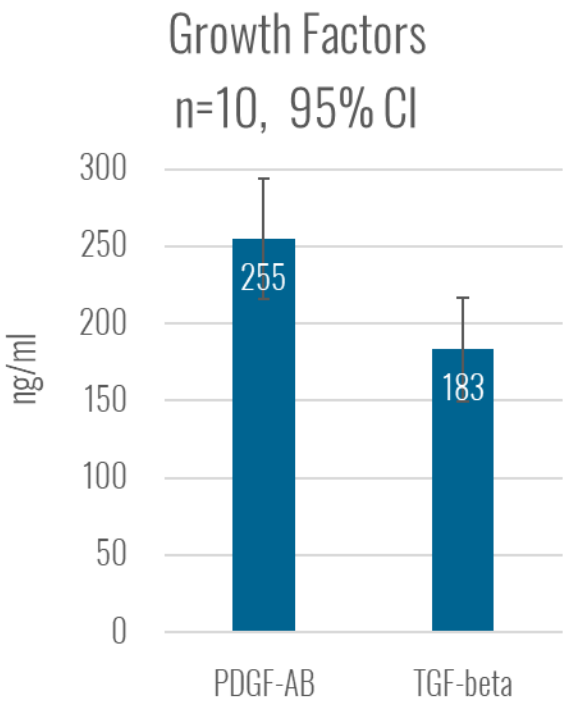


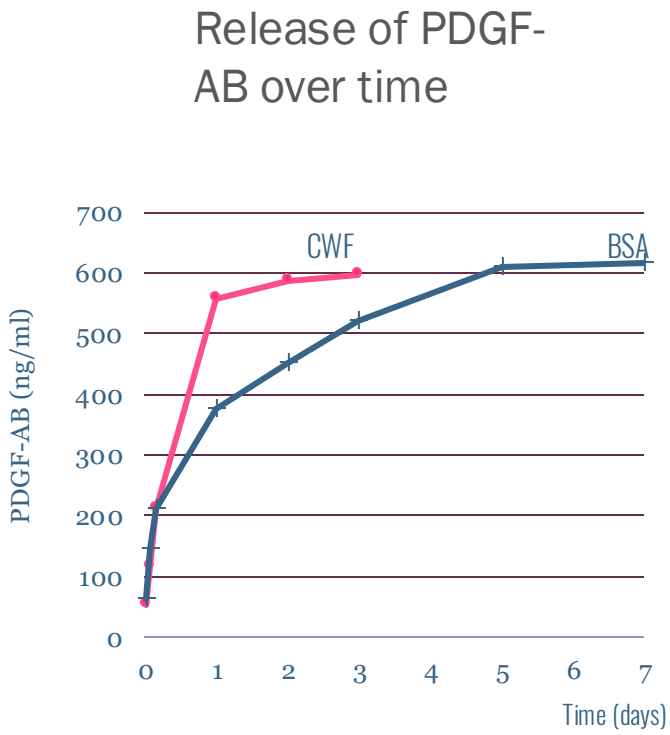
Microscope recording of cells in an autologous MLPF patch

Lundquist et al (2013) Wound Repair and Regeneration. Thomsen et al. (2016), Clinical and Experimental Immunology. Schmidt et al. (2017)C Patch derived autologous immune cells delivers immune responses appropriate for the treatment of Diabetic Foot Ulcers, Poster DLES at Harvard Medical School.

Role of Platelets in Wound Healing

- In-vitro evidence has detected more than 800 different proteins, cytokines, and growth factors released from the autologous MLPF patch
- PDGF-AB is known to stimulate granulation tissue formation, re-epithelialization, matrix formation, stimulates angiogenesis, wound contraction
- TGF-α known to increase keratinocyte migration and proliferation
- TGF-β known to be involved in collagen production, granulation tissue formation, keratinocytes migration
- VEGF – known to stimulate angiogenesis, granulation tissue formation





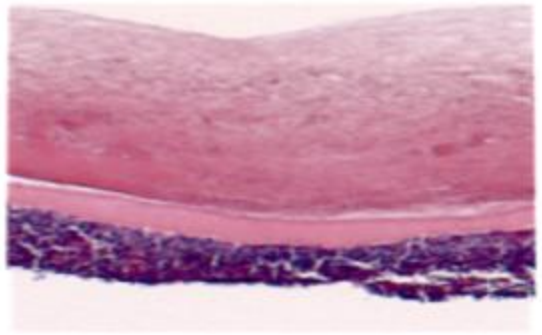
Lundquist et al (2013) Wound Repair and Regeneration
In-vitro data on file
PDGF:Platelet Derived Growth Factor, TGF: Transforming Growth Factor, VEGF: Vascular Endothelial Growth Factor, CWF: Chronic Wound Fluid, BSA: Bovine Serum Albumin (control protein)

NOT PRP! Composition, Content, and Process Advantage over PRP

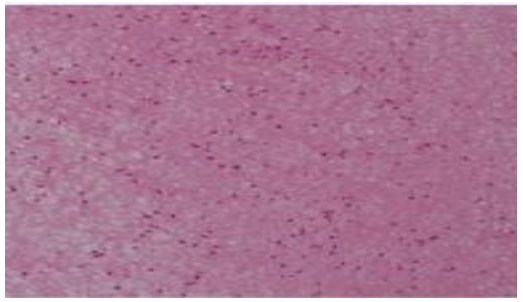
Autologous MLPF Patch vs PRP

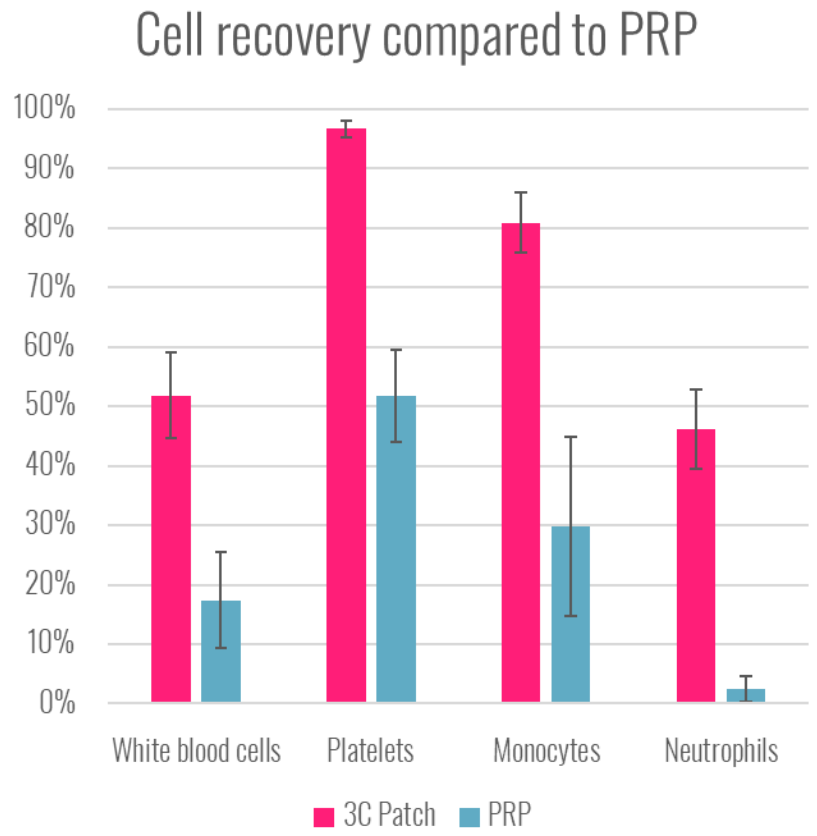
- 3-layer structure vs homogenous
  - Increased cell and growth factor release to the wound bed
  - Release living immune cells key in wound healing
  - Easy application
- Automated hard spin process
  - Higher and more consistent cell recovery
  - Less hands-on time
- Includes growth factors and key signaling molecules from platelets and immune cells
- Prospective randomized clinical data

Patch



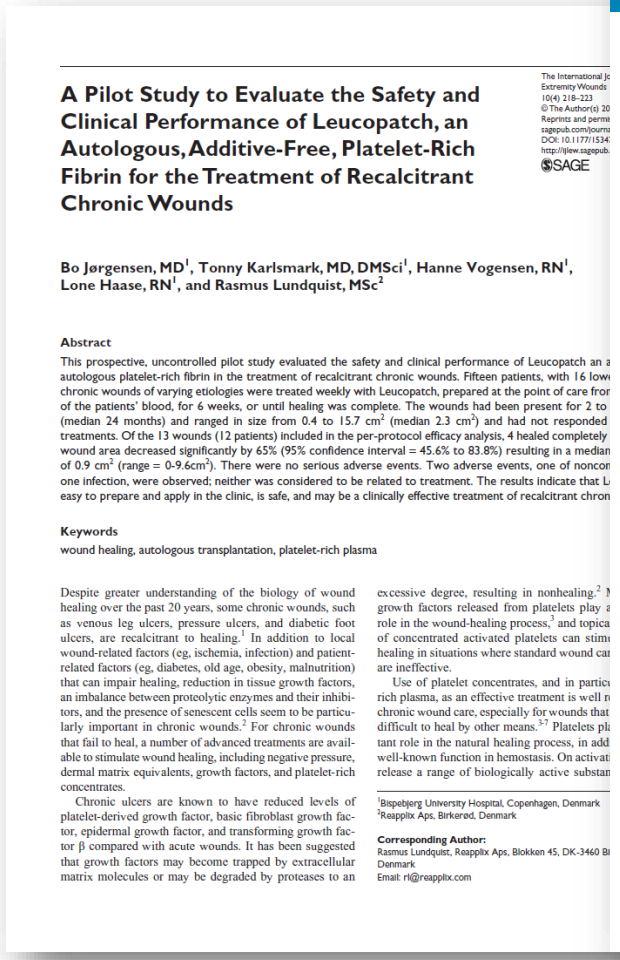
PRP





Lundquist et al (2013) Wound Repair and Regeneration, SAWC Spring 2022

Clinical Studies of 3C Patch



A Pilot Study to Evaluate the Safety and Clinical Performance of Leucopatch, an Autologous, Additive-Free, Platelet-Rich Fibrin for the Treatment of Recalcitrant Chronic Wounds

Bo Jørgensen, MD[1], Tonny Karlsmark, MD, DMSci[1], Hanne Vogensen, RN[1], Lone Haase, RN[1], and Rasmus Lundquist, MSc[2]

Abstract

This prospective, uncontrolled pilot study evaluated the safety and clinical performance of Leucopatch an a autologous platelet-rich fibrin in the treatment of recalcitrant chronic wounds. Fifteen patients, with 16 lowe chronic wounds of varying etiologies were treated weekly with Leucopatch, prepared at the point of care fro of the patients' blood, for 6 weeks, or until healing was complete. The wounds had been present for 2 to (median 24 months) and ranged in size from 0.4 to 15.7 cm^2 (median 2.3 cm^2) and had not responded treatments. Of the 13 wounds (12 patients) included in the per-protocol efficacy analysis, 4 healed completely wound area decreased significantly by 65% (95% confidence interval = 45.6% to 83.8%) resulting in a median of 0.9 cm^2 (range = 0-9.6cm^2). There were no serious adverse events. Two adverse events, one of noncon one infection, were observed; neither was considered to be related to treatment. The results indicate that L easy to prepare and apply in the clinic, is safe, and may be a clinically effective treatment of recalcitrant chron

Keywords

wound healing, autologous transplantation, platelet-rich plasma

Despite greater understanding of the biology of wound healing over the past 20 years, some chronic wounds, such as venous leg ulcers, pressure ulcers, and diabetic foot ulcers, are recalcitrant to healing.[1] In addition to local wound-related factors (eg, ischemia, infection) and patient-related factors (eg, diabetes, old age, obesity, malnutrition) that can impair healing, reduction in tissue growth factors, an imbalance between proteolytic enzymes and their inhibitors, and the presence of senescent cells seem to be particularly important in chronic wounds.[2] For chronic wounds that fail to heal, a number of advanced treatments are available to stimulate wound healing, including negative pressure, dermal matrix equivalents, growth factors, and platelet-rich concentrates.

Chronic ulcers are known to have reduced levels of platelet-derived growth factor, basic fibroblast growth factor, epidermal growth factor, and transforming growth factor β compared with acute wounds. It has been suggested that growth factors may become trapped by extracellular matrix molecules or may be degraded by proteases to an excessive degree, resulting in nonhealing.[2] growth factors released from platelets play a role in the wound-healing process,[3] and topica of concentrated activated platelets can stim healing in situations where standard wound ca are ineffective.

Use of platelet concentrates, and in partic rich plasma, as an effective treatment is well n chronic wound care, especially for wounds that difficult to heal by other means.[3-7] Platelets pl tant role in the natural healing process, in add well-known function in hemostasis. On activat release a range of biologically active substan

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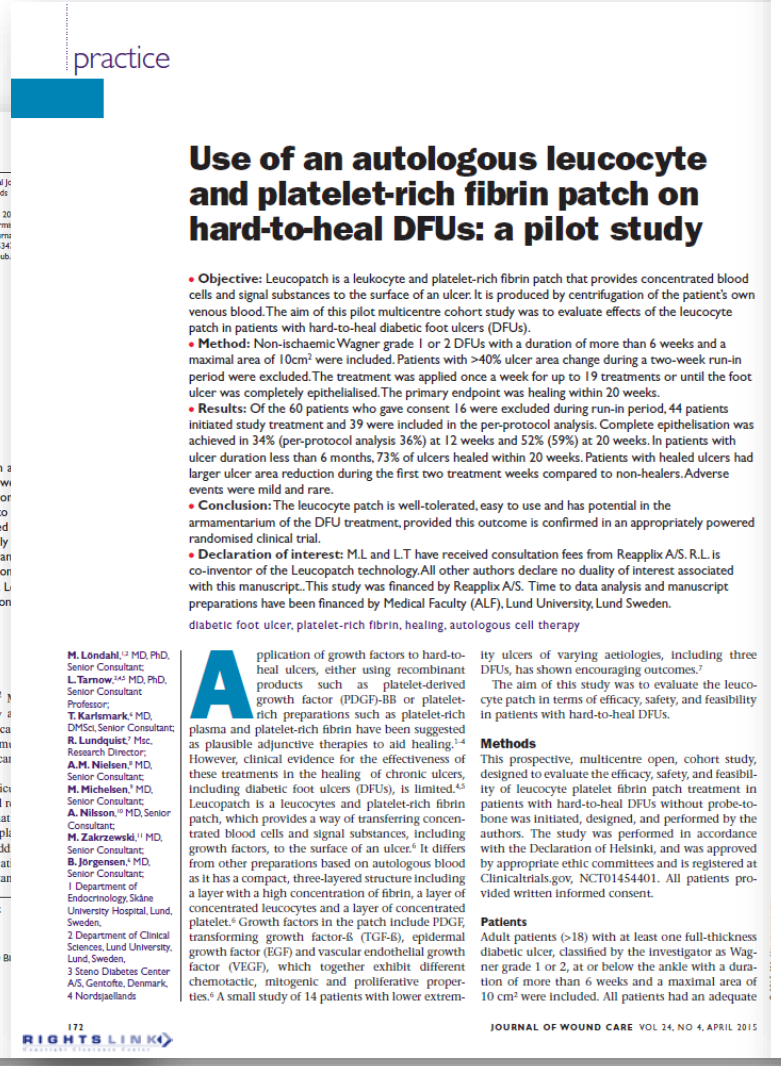

practice

Use of an autologous leucocyte and platelet-rich fibrin patch on hard-to-heal DFUs: a pilot study

• **Objective:** Leucopatch is a leukocyte and platelet-rich fibrin patch that provides concentrated blood cells and signal substances to the surface of an ulcer. It is produced by centrifugation of the patient's own venous blood. The aim of this pilot multicentre cohort study was to evaluate effects of the leucocyte patch in patients with hard-to-heal diabetic foot ulcers (DFUs).
• **Method:** Non-ischaemic Wagner grade 1 or 2 DFUs with a duration of more than 6 weeks and a maximal area of 10cm^2 were included. Patients with >40% ulcer area change during a two-week run-in period were excluded. The treatment was applied once a week for up to 19 treatments or until the foot ulcer was completely epithelialised. The primary endpoint was healing within 20 weeks.
• **Results:** Of the 60 patients who gave consent 16 were excluded during run-in period, 44 patients initiated study treatment and 39 were included in the per-protocol analysis. Complete epithelisation was achieved in 34% (per-protocol analysis 36%) at 12 weeks and 52% (59%) at 20 weeks. In patients with ulcer duration less than 6 months, 73% of ulcers healed within 20 weeks. Patients with healed ulcers had larger ulcer area reduction during the first two treatment weeks compared to non-healers. Adverse events were mild and rare.
• **Conclusion:** The leucocyte patch is well-tolerated, easy to use and has potential in the armamentarium of the DFU treatment, provided this outcome is confirmed in an appropriately powered randomised clinical trial.
• **Declaration of interest:** M.L and L.T have received consultation fees from Reapplix A/S. R.L. is co-inventor of the Leucopatch technology. All other authors declare no duality of interest associated with this manuscript. This study was financed by Reapplix A/S. Time to data analysis and manuscript preparations have been financed by Medical Faculty (ALF), Lund University, Lund Sweden.

diabetic foot ulcer, platelet-rich fibrin, healing, autologous cell therapy

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4 Nordsjaellands

Application of growth factors to hard-to-heal ulcers, either using recombinant products such as platelet-derived growth factor (PDGF)-BB or platelet-rich preparations such as platelet-rich plasma and platelet-rich fibrin have been suggested as plausible adjunctive therapies to aid healing.[1-4] However, clinical evidence for the effectiveness of these treatments in the healing of chronic ulcers, including diabetic foot ulcers (DFUs), is limited.[4,5] Leucopatch is a leucocytes and platelet-rich fibrin patch, which provides a way of transferring concentrated blood cells and signal substances, including growth factors, to the surface of an ulcer.[6] It differs from other preparations based on autologous blood as it has a compact, three-layered structure including a layer with a high concentration of fibrin, a layer of concentrated leucocytes and a layer of concentrated platelet.[6] Growth factors in the patch include PDGF, transforming growth factor-ß (TGF-ß), epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF), which together exhibit different chemotactic, mitogenic and proliferative properties.[6] A small study of 14 patients with lower extremity ulcers of varying aetiologies, including three DFUs, has shown encouraging outcomes.[7]

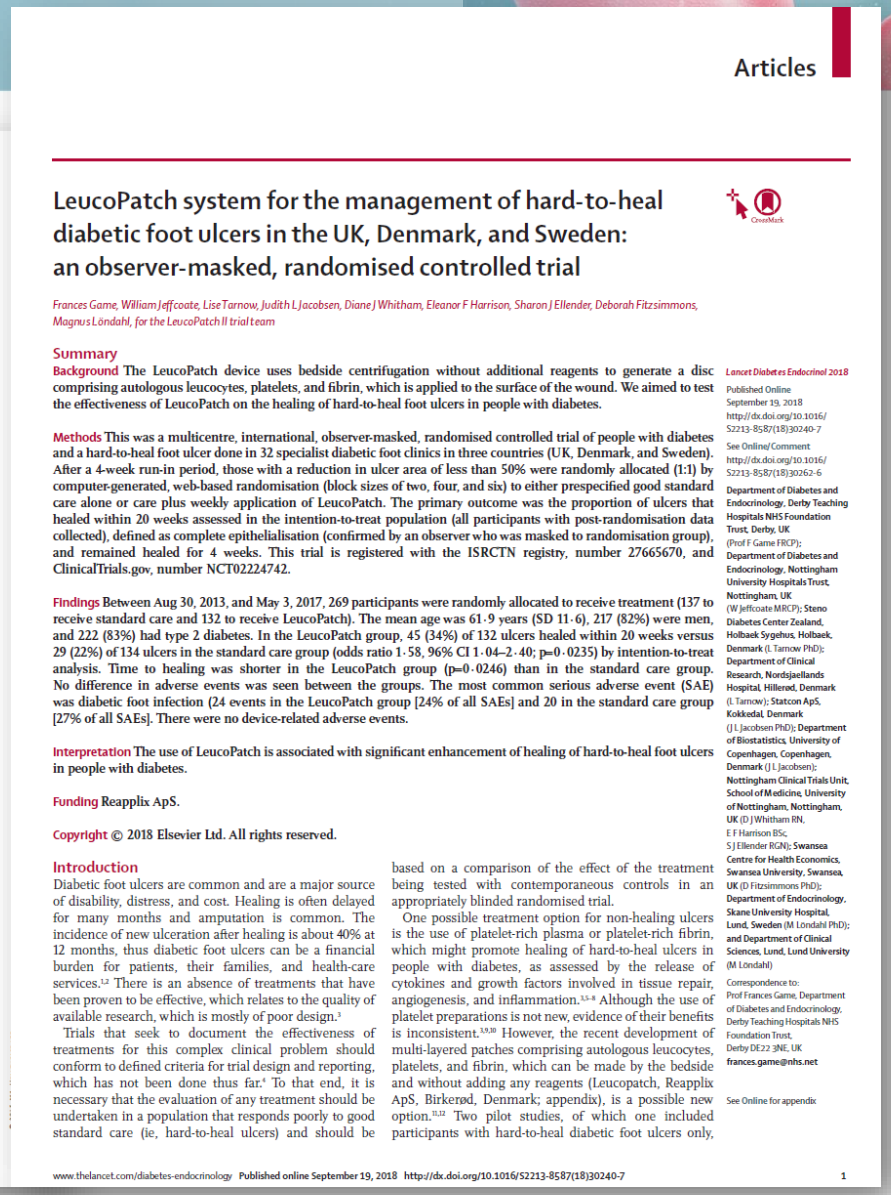
The aim of this study was to evaluate the leucocyte patch in terms of efficacy, safety, and feasibility in patients with hard-to-heal DFUs.

Methods

This prospective, multicentre open, cohort study, designed to evaluate the efficacy, safety, and feasibility of leucocyte platelet fibrin patch treatment in patients with hard-to-heal DFUs without probe-to-bone was initiated, designed, and performed by the authors. The study was performed in accordance with the Declaration of Helsinki, and was approved by appropriate ethic committees and is registered at Clinicaltrials.gov, NCT01454401. All patients provided written informed consent.

Patients

Adult patients (>18) with at least one full-thickness diabetic ulcer, classified by the investigator as Wagner grade 1 or 2, at or below the ankle with a duration of more than 6 weeks and a maximal area of 10 cm^2 were included. All patients had an adequate



LeucoPatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked, randomised controlled trial

Frances Game, William Jeffcoate, Lise Tarnow, Judith L Jacobsen, Diane J Whitham, Eleanor F Harrison, Sharon J Ellender, Deborah Fitzsimmons, Magnus Löndahl, for the LeucoPatch II trial team

Summary

Background The LeucoPatch device uses bedside centrifugation without additional reagents to generate a disc comprising autologous leucocytes, platelets, and fibrin, which is applied to the surface of the wound. We aimed to test the effectiveness of LeucoPatch on the healing of hard-to-heal foot ulcers in people with diabetes.

Methods This was a multicentre, international, observer-masked, randomised controlled trial of people with diabetes and a hard-to-heal foot ulcer done in 32 specialist diabetic foot clinics in three countries (UK, Denmark, and Sweden). After a 4-week run-in period, those with a reduction in ulcer area of less than 50% were randomly allocated (1:1) by computer-generated, web-based randomisation (block sizes of two, four, and six) to either prespecified good standard care alone or care plus weekly application of LeucoPatch. The primary outcome was the proportion of ulcers that healed within 20 weeks assessed in the intention-to-treat population (all participants with post-randomisation data collected), defined as complete epithelialisation (confirmed by an observer who was masked to randomisation group), and remained healed for 4 weeks. This trial is registered with the ISRCTN registry, number 27665670, and ClinicalTrials.gov, number NCT02224742.

Findings Between Aug 30, 2013, and May 3, 2017, 269 participants were randomly allocated to receive treatment (137 to receive standard care and 132 to receive LeucoPatch). The mean age was 61·9 years (SD 11·6), 217 (82%) were men, and 222 (83%) had type 2 diabetes. In the LeucoPatch group, 45 (34%) of 132 ulcers healed within 20 weeks versus 29 (22%) of 134 ulcers in the standard care group (odds ratio 1·58, 96% CI 1·04–2·40; p=0·0235) by intention-to-treat analysis. Time to healing was shorter in the LeucoPatch group (p=0·0246) than in the standard care group. No difference in adverse events was seen between the groups. The most common serious adverse event (SAE) was diabetic foot infection (24 events in the LeucoPatch group [24% of all SAEs] and 20 in the standard care group [27% of all SAEs]. There were no device-related adverse events.

Interpretation The use of LeucoPatch is associated with significant enhancement of healing of hard-to-heal foot ulcers in people with diabetes.

Funding Reapplix ApS.

Introduction

Diabetic foot ulcers are common and are a major source of disability, distress, and cost. Healing is often delayed for many months and amputation is common. The incidence of new ulceration after healing is about 40% at 12 months, thus diabetic foot ulcers can be a financial burden for patients, their families, and health-care services.[1,2] There is an absence of treatments that have been proven to be effective, which relates to the quality of available research, which is mostly of poor design.[3] Trials that seek to document the effectiveness of treatments for this complex clinical problem should conform to defined criteria for trial design and reporting, which has not been done thus far.[4] To that end, it is necessary that the evaluation of any treatment should be undertaken in a population that responds poorly to good standard care (ie, hard-to-heal ulcers) and should be based on a comparison of the effect of the treatment being tested with contemporaneous controls in an appropriately blinded randomised trial.

One possible treatment option for non-healing ulcers is the use of platelet-rich plasma or platelet-rich fibrin, which might promote healing of hard-to-heal ulcers in people with diabetes, as assessed by the release of cytokines and growth factors involved in tissue repair, angiogenesis, and inflammation.[3,5–8] Although the use of platelet preparations is not new, evidence of their benefits is inconsistent.[3,9,10] However, the recent development of multi-layered patches comprising autologous leucocytes, platelets, and fibrin, which can be made by the bedside and without adding any reagents (Leucopatch, Reapplix ApS, Birkerød, Denmark; appendix), is a possible new option.[11,12] Two pilot studies, of which one included participants with hard-to-heal diabetic foot ulcers only,

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See Online/Comment http://dx.doi.org/10.1016/S2213-8587(18)30262-6

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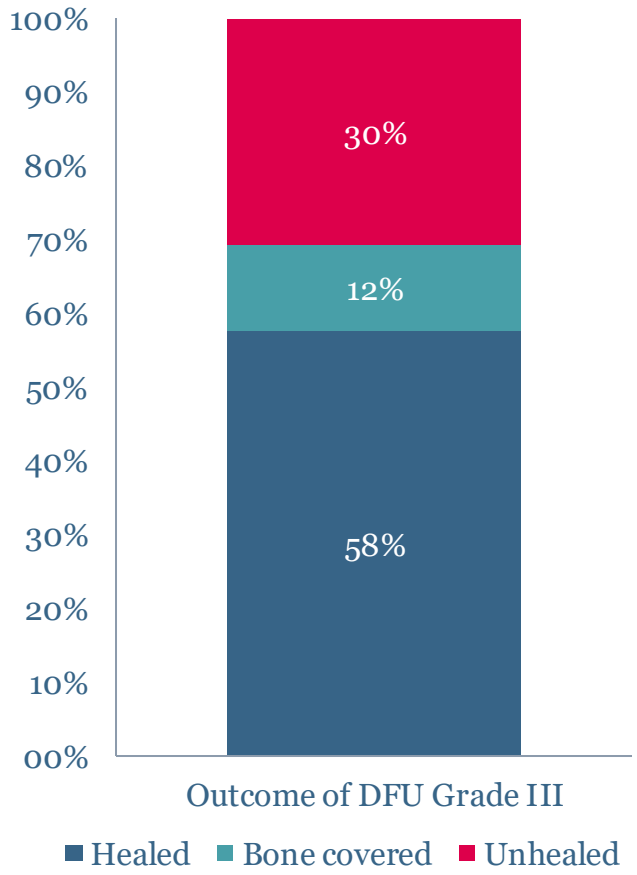
See Online for appendix

*3C Patch was previously known as LeucoPatch

Autologous MLPF Patch Case Series: Treating Probe to Bone Ulcers

Autologous MLPF Patch has been investigated for use on exposed bone

- **Purpose:** To evaluate the feasibility of using autologous patch in the treatment of diabetic foot ulcers with probe to bone (≥Wagner grade 3)
- **Method:** The outcome of 3C Patch treatment on 26 ulcers on 22 patients was analyzed
- **Results**
  - Median ulcer duration was 26 wks, and the median number of treatments was 8
  - **Bone was covered in 18 ulcers of which 15 healed with complete epithelialization**



Löndahl et al – ADA 2021

The LEUCOpatch* II Trial

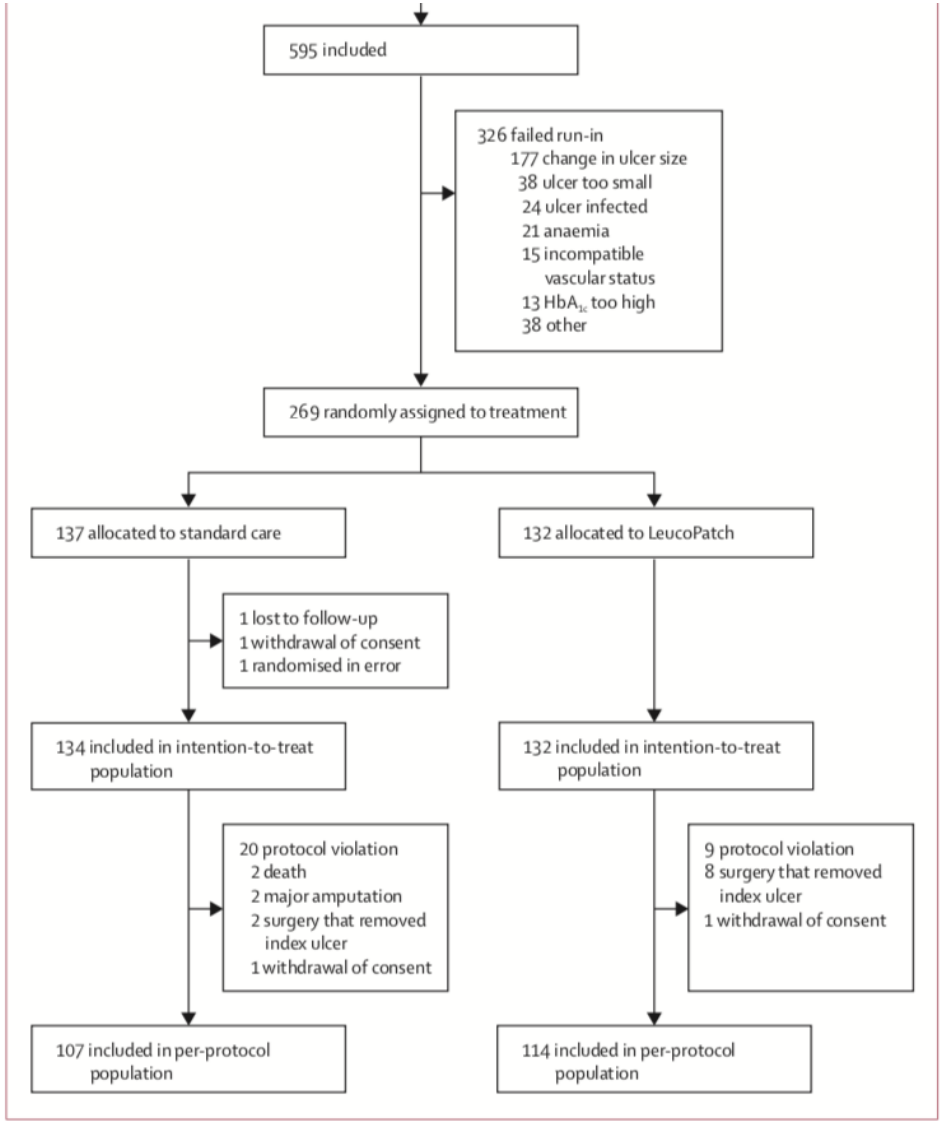
An Investigator-driven randomized controlled trial

Study details:

- 269 patient randomized across 32 centres
- ***Only study with a full 4-wk run-in period*** with <50% wound area reduction
- Primary endpoint
- Proportion of patients with complete wound closure within 20 wks

Hard-to-heal Diabetic Foot Ulcers

- 595 consented patients
- 326 excluded during run-in
  - 177 healed >50% in 4 wks
- 269 patients randomized
- Well matched patient populations

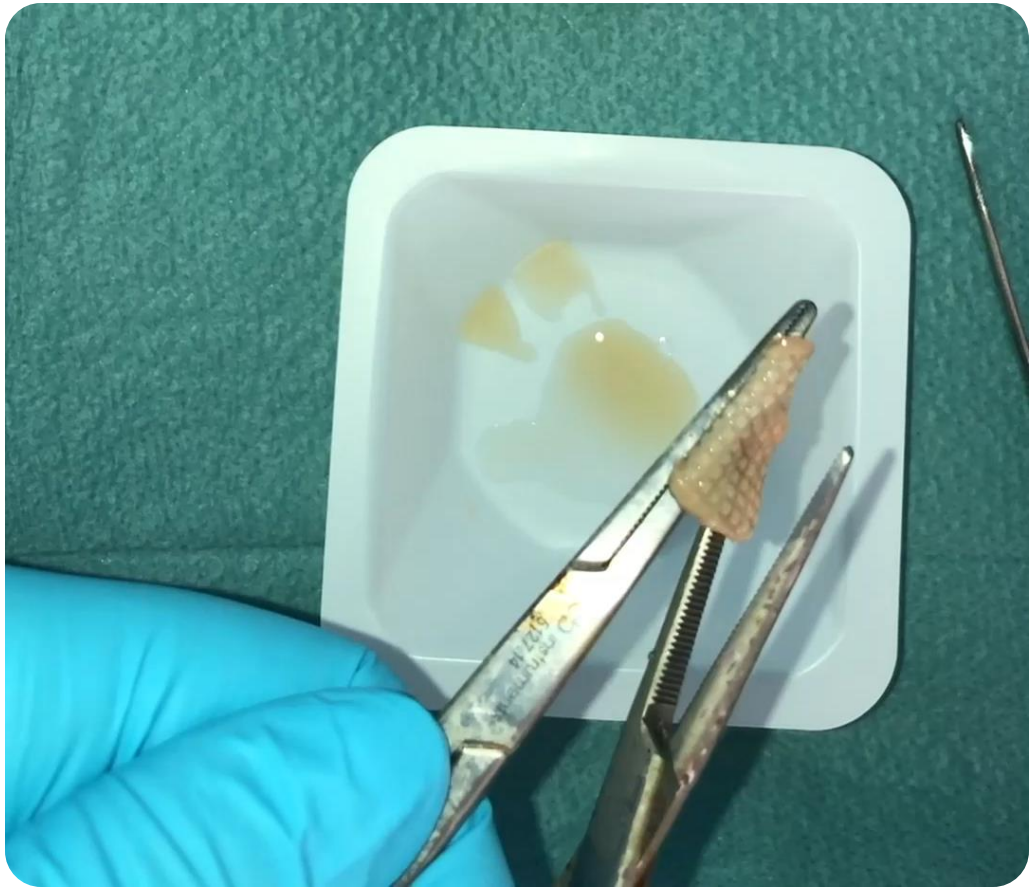


*3C Patch was previously known as LeucoPatch

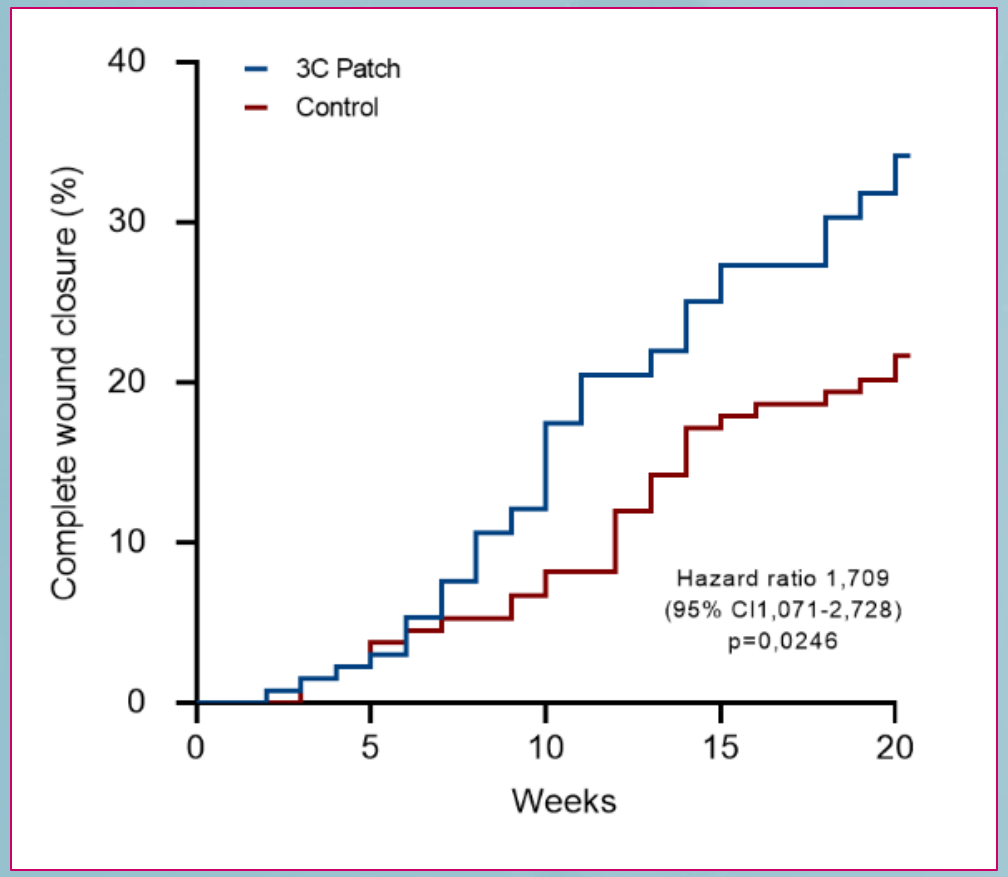
Game et al., 2018, Lancet Diabetes Endocrinology. 2018;6(11):870-878

Relevant Patient Population

- Non-responding for 4 wks
- Wagner Grade 3 wounds included
- ABI down to 0.5
- “Real” wound care patients from >30 centers
- Best standard of care including debridement, offloading, NPWT, protease inhibitors, etc.



Autologous MLPF Patch Improves Healing of Hard-to-Heal Diabetic Foot Ulcers



- Graph is demonstrating time to healing
- Healing was defined as complete epithelization without any drainage for at least 4 weeks
- 58% more patients healed with an autologous patch
- Interestingly enough, the wounds in the autologous patch group were larger than the wounds in the control
- Further data analysis was conducted and it was found that if all things had been equal, the autologous patch group was 89% more likely to heal
- Autologous MLPF patch group also healed progressively faster in the first 12 wks

International Working Group of the Diabetic Foot

IWGDF GUIDANCE May 25, 2019 and Updated 2023 Guidelines – Wound Healing Interventions Guideline:

19. With the exception of the autologous leucocyte, platelet, and fibrin patch we suggest not using autologous platelets therapy (including blood bank derived platelets) as an adjunct therapy to standard of care. (Conditional; Low)

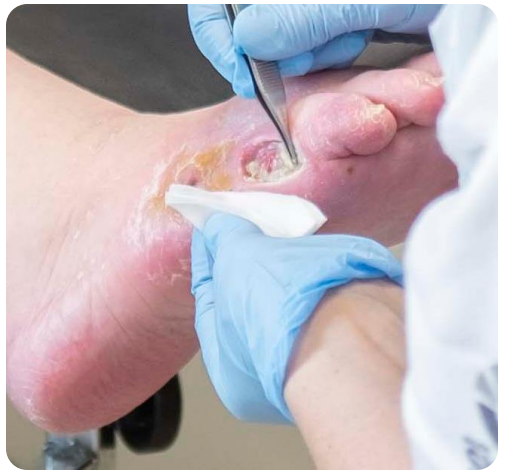
20. Consider the use of autologous leucocyte, platelet and fibrin patch for diabetes-related foot ulcers as an adjunctive therapy to standard of care, where best standard of care alone has been ineffective, and where the resources and expertise exist for the regular venipuncture required. (Conditional; Moderate)

2019 IWGDF Guidelines on the Prevention and Management of Diabetic Foot Disease
Gerry Rayman, Prashant Vas , Ketan Dhatariya, Vicki Driver, Agnes Hartemann, Magnus Londahl, Alberto Piaggesi, Jan Apelqvist, Chris Attinger, Fran Game on behalf of the International Working Group of the Diabetic Foot (IWGDF)

Autologous MLPF Patch Procedure

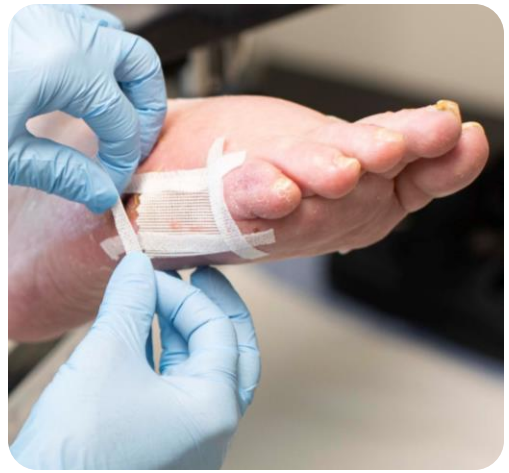
Draw blood

Place the device in the centrifuge



Clean and debride the wound

Remove the autologous patch from the device



Apply the patch and dress the wound

Factors that Improve the Treatment Outcome

- The wound is debrided to bleeding before autologous patch is applied
- Appropriate offloading modalities are key
- Ensure adequate perfusion for wound healing
- Secondary dressing change frequency depends on exudate (typically decreases after a few wks of treatment)
- Consider from week-to-week if autologous patch is effective

Patient and Staff Adoption of the Autologous MLPF Patch

Implementing Autologous MLPF Pa

- Staff training
- Space requirements
- Patient scheduling

Clinical workflow

- Patients are allowed up to 20 wks of treatment

Patients' acceptance

- Well-adapted to receive weekly blood draws
- Patient involvement and wound improvement

The Impact of an Autologous Multilayered Patch on the Perfusion of a Chronic Wound

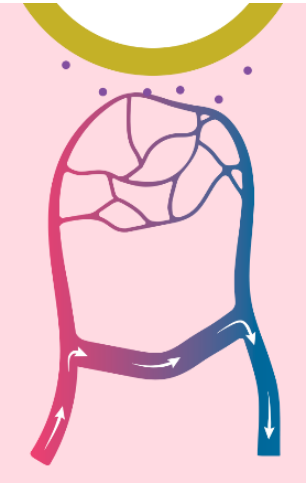
Anthony Tickner, DPM, FACCWS, FAPWH, FRCPS
President at Massachusetts Foot And Ankle Society
Medical Director at Saint Vincent Hospital/RestorixHealth Wound Healing Center
Worcester, MA

Diabetic Foot Ulcers Are Hard to Heal

DFUs are a common and severe complication of diabetes that occur as diabetes impairs peripheral blood flow and stalls the healing cascade

- Over time, excess blood glucose causes
  - Impaired blood vessels
  - Neuropathy that often leads to ulcers
- Impaired wound healing in diabetics
  - Impaired shunting
  - Impaired vasodilation
  - Leading to sub-optimal inflammation
- Can lead to
  - Tissue infection
  - Bone infection
  - Amputation

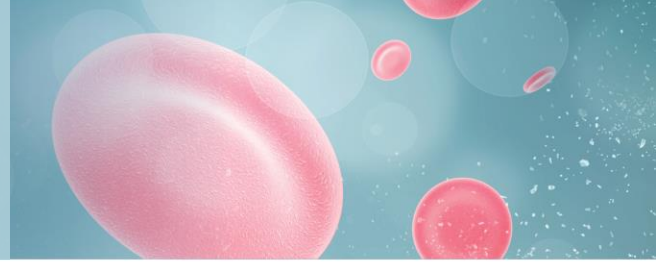
AV shunting is part of the normal healing response. Immune cells, platelets, and growth factors reach the wound



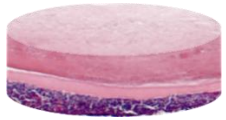
In neuropathic patients, no shunting is seen, leading to a poor healing response

Jörneskog 2012, Scandinavian Journal of Surgery, Eming, et al. 2007 J. Invest. Dermatol.

What a Wound Needs to Heal: The Healing Phases

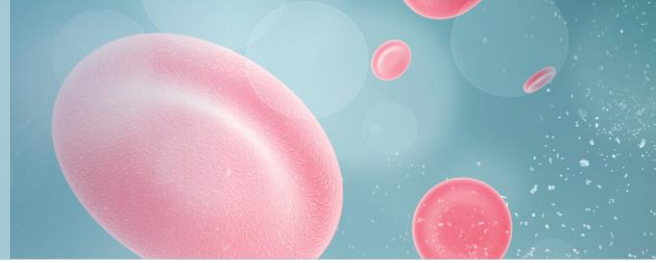


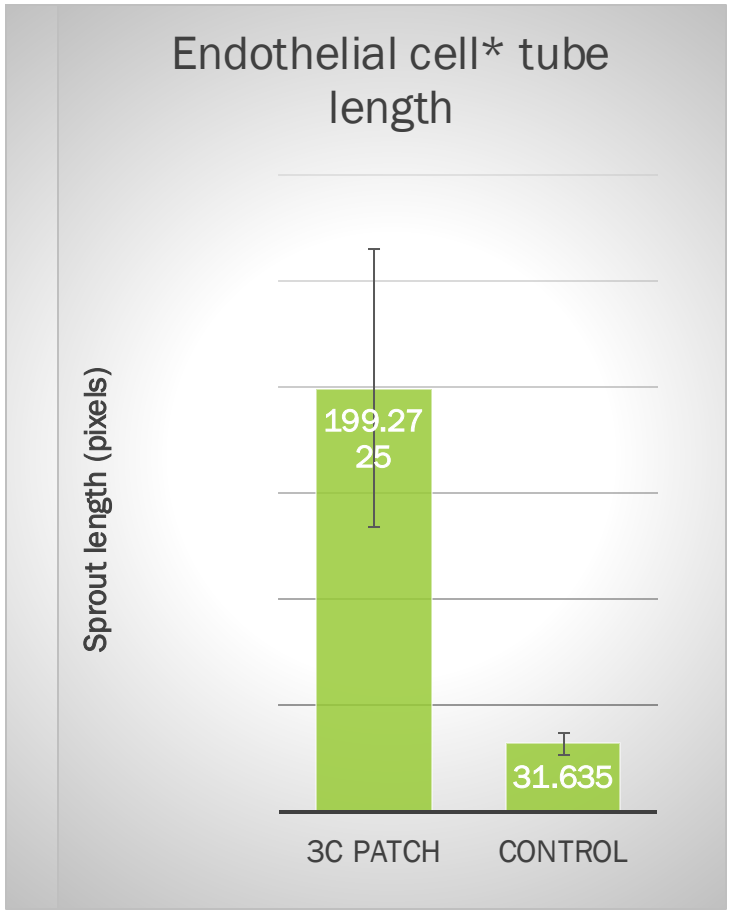
	Coagulation	Inflammation	Proliferation	Epithelization	Remodeling
Healing components	• Platelets, fibrin	• Leukocytes - Neutrophils - Monocytes - lymphocytes	• Fibroblast proliferation • Collagen production • Angiogenesis	• Keratinocytes	• Collagen remodeling
Why	• Stop bleeding • Start activation of surrounding cells to divide and migrate	• Cells to clean the wound from dead tissue, prevent infection and orchestrate healing	• ECM and tissue formation • Blood vessel formation	• Wound closure	• Strengthen tissue
What the Patch Brings	• **98% platelet recovery** • **Coagulation factors (fibrin and thrombin)** • **Growth factors**	• **High cell recovery:** **85% Monocytes** **77% Lymphocytes** **55% Neutrophils** • **Pro- and anti-inflammatory cytokines**	• **High growth factor levels** • **Activation of fibroblast cells and collagen production.** • **Endothelial cell growth**	• **Increased keratinocyte growth and migration**	

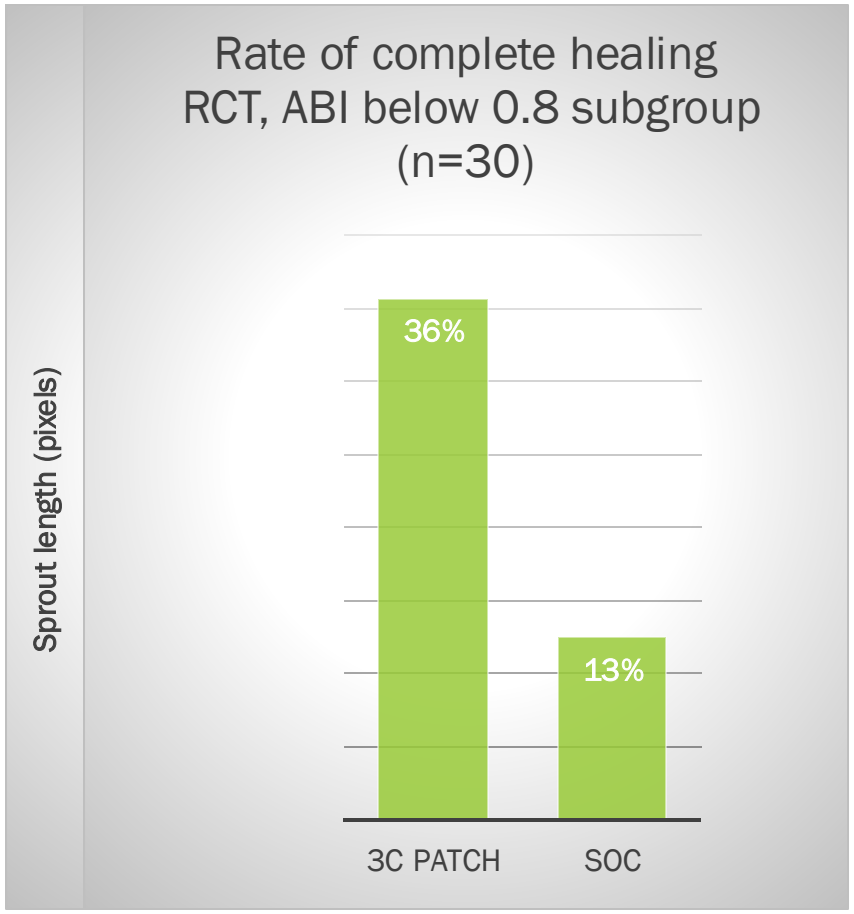


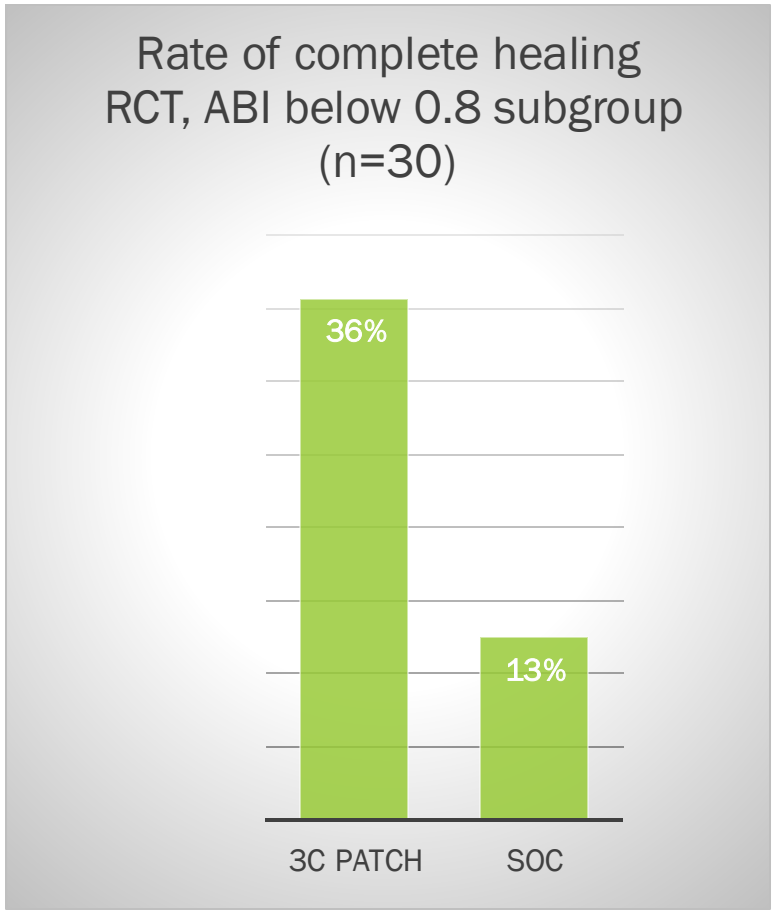
Leukocyte platelet & fibrin 3-layer patch

Autologous MLPF Patch Effects On Angiogenesis









* HUVEC (Human umbilical vein endothelial cells) grown in 10% 3C Patch conditioned media or growth media. Tube length determined by microscopy.

Schmidt et al. , Lundquist et al (2013) Wound Repair and Regeneration

Game F., Jeffcoate W., ..., Löndahl M., LeucoPatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked randomized controlled trial. Lancet Diabetes Endocrinol. 2018 Nov;6(11):870-878.

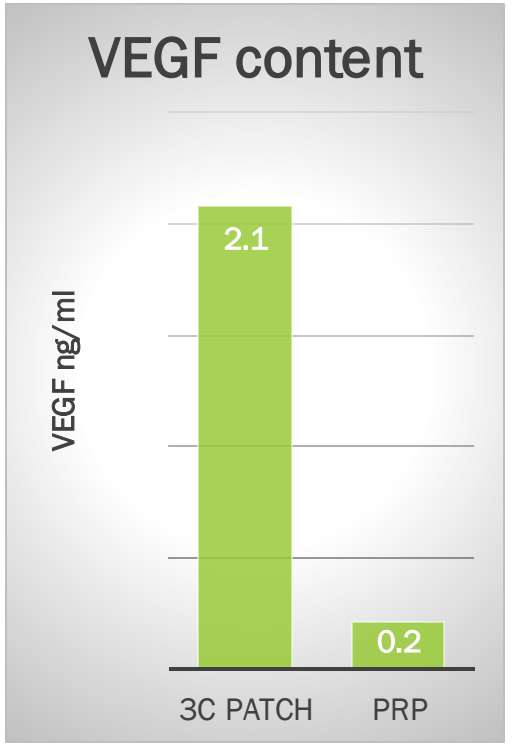
Autologous MLPF Patch: Growth Factor Release

Table 3. Comparison patch and platelet rich plasma extracts

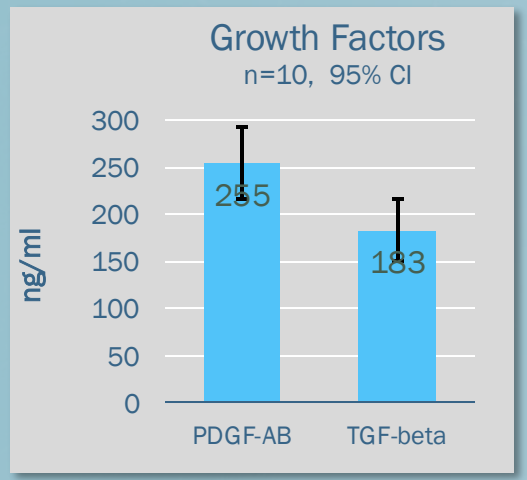
		Growth factors released (range)	Growth factor released per 10^6 platelets in starting blood sample (pg) (range)	Growth factor released per 10^6 platelets in final product (pg) (range)	Growth factors* released per cm^2 (ng)	
PDGF-AB	Patch	171.5 ng (123–257)	40.1 (37–48)	40.9 (37–48)	35	
	PRP	66.2 ng/mL (58–72)	31.6 (27–39)	66.2 (58–72)	13	3x
VEGF	Patch	2.08 ng (1.16–5.09)	0.44 (0.30–0.78)	0.45 (0.30–0.78)	0.36	
	PRP	0.21 ng/mL (0.018–0.59)	0.09 (0.01–0.23)	0.209 (0.018–0.59)	0.042	8x
IL-8	Patch	1.78 ng (0.57–3.65)	0.41 (0.18–0.93)	0.42 (0.18–0.93)	0.42	
	PRP	0.0063 ng/mL (0–0.108)	0.003 (0–0.005)	0.006 (0–0.011)	0.0013	300x

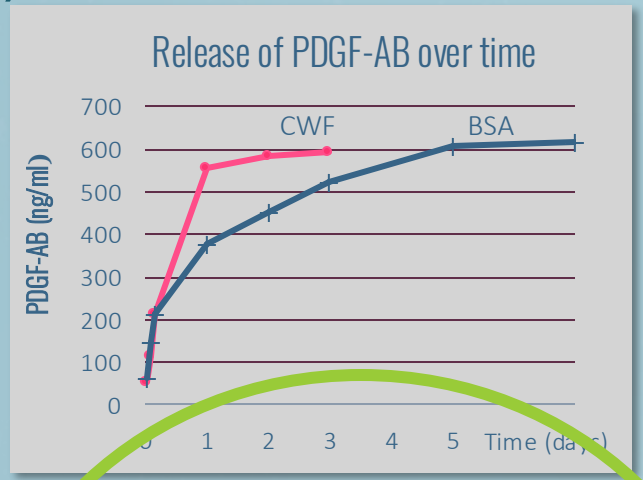
*Compared with the application of a 2 mm layer of PRP.

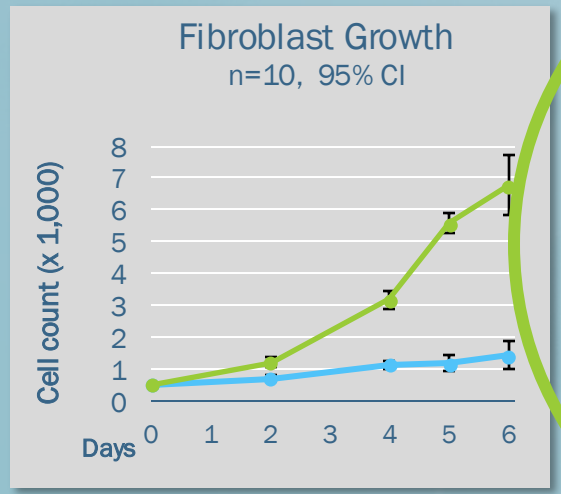
IL-8, interleukin 8; PDGF-AB, platelet-derived growth factor AB; PRP, platelet-rich plasma; VEGF, vascular endothelial growth factor.

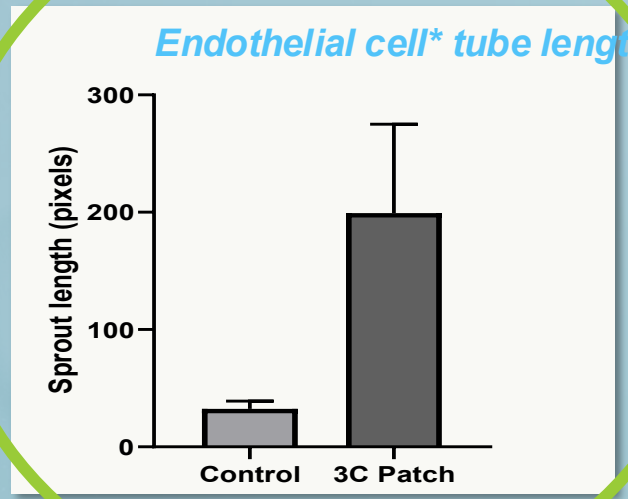


Autologous MLPF Patch Promotes Blood Vessel Formation, Skin, and Connective Tissue Cell Growth







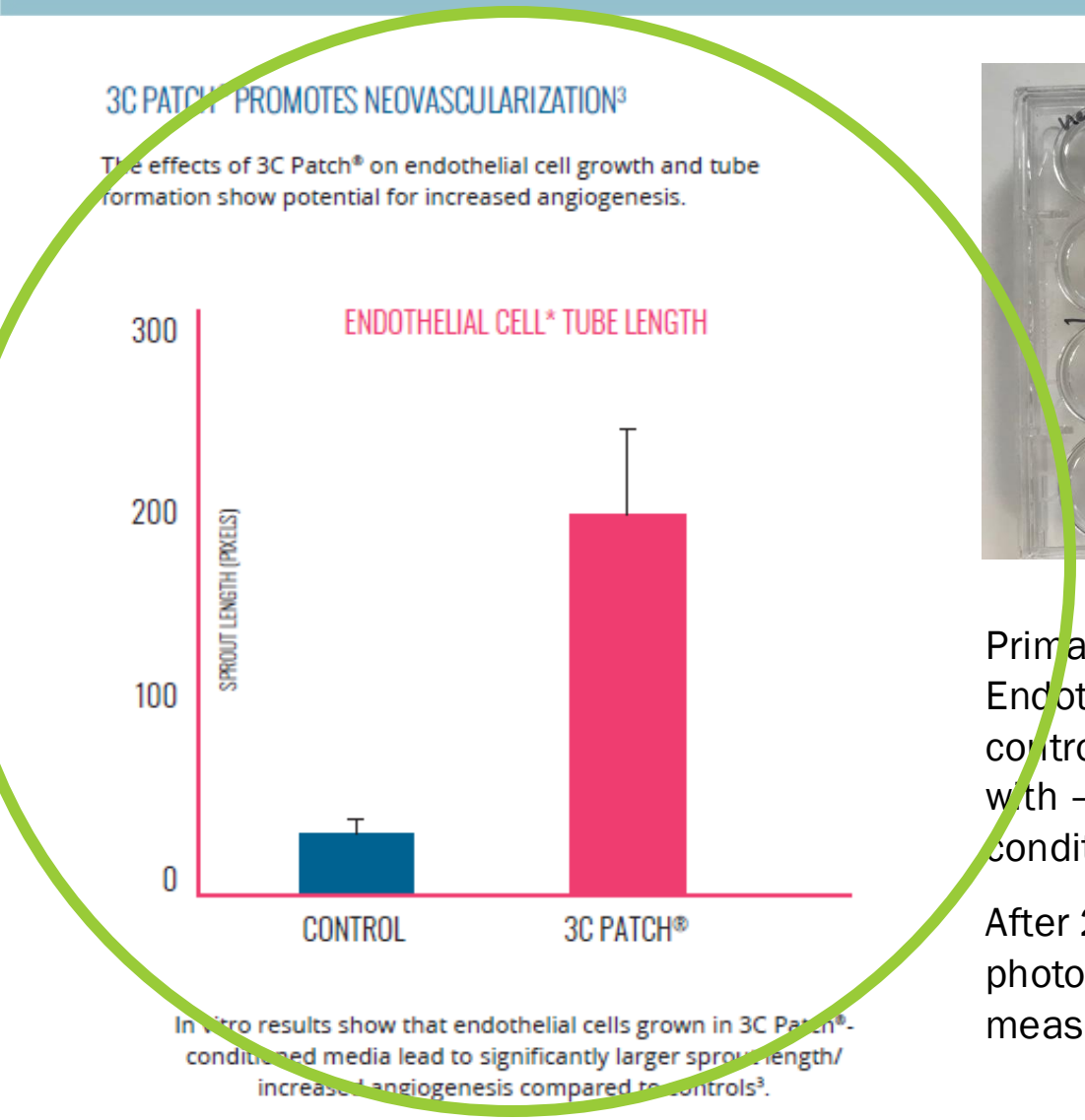


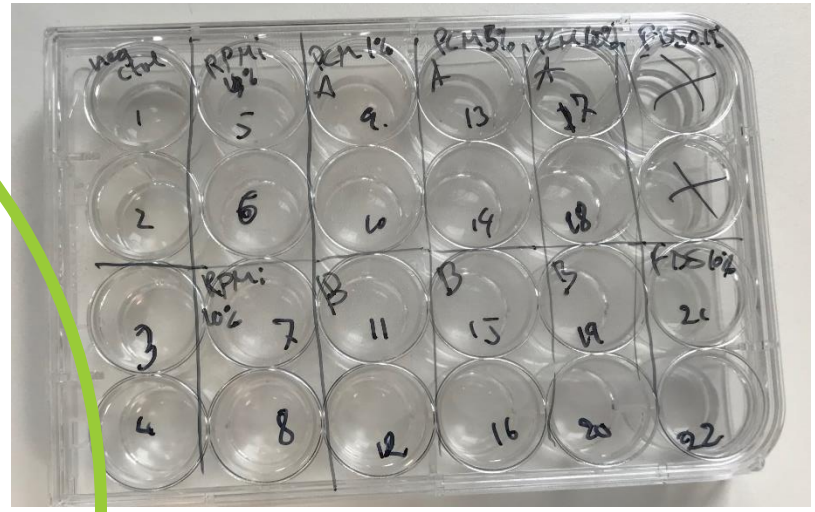
Proliferation phase

- Continued release of high growth factor levels
- Activation of fibroblast cells
- Endothelial cell growth
  - The growth and formation of blood vessels by endothelial cells show potential for increased angiogenesis

* HUVEC (Human umbilical vein endothelial cells) grown in 10% 3C Patch conditioned media or growth media. Tube length determined by microscopy.
Schmidt et al. , Lundquist et al (2013) Wound Repair and Regeneration

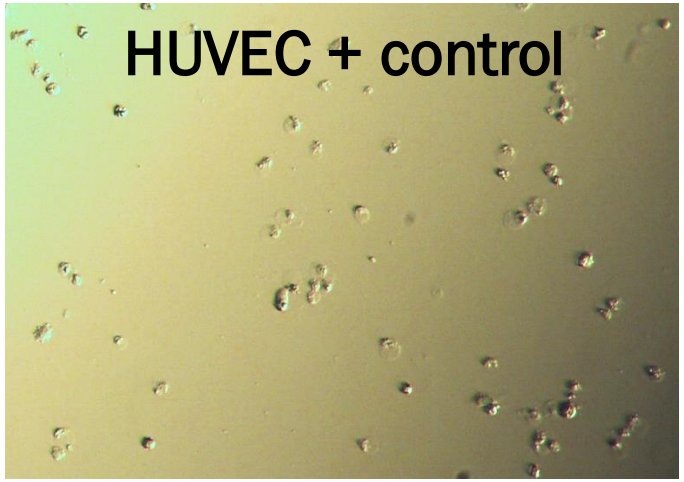
Autologous MLPF Patch: Neovascularization

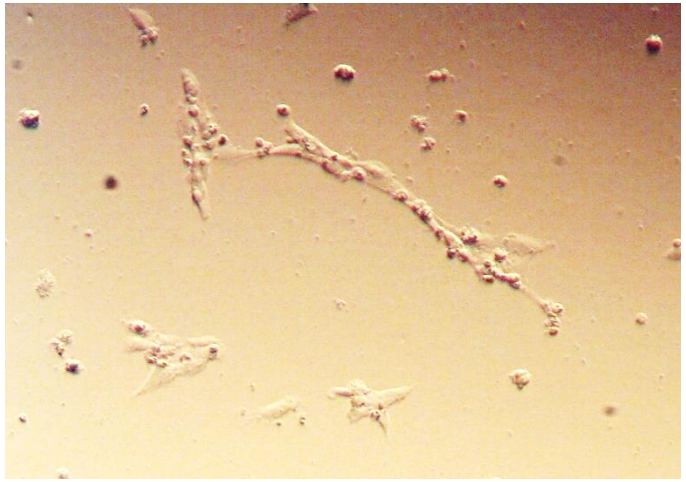




Primary Human Umbilical Vein Endothelial Cells (HUVECs) grown in control medium (200PRF) in the lab with – or without – 3C Patch conditioned medium.

After 20 hrs cultures are photographed and “tube lengths” measured.





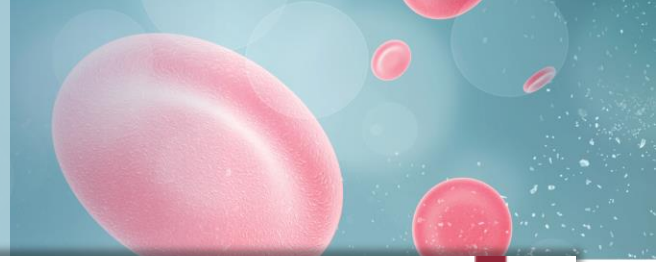
HUVEC + 10% autologous MLPF patch conditioned media

Large 269 Patient RCT Published In *The Lancet Diabetes & Endocrinology*

Large International RCT

Very challenging patient population:

- Patients whose ulcers did not reduce in area more than 50% over a 4-wk run-in period despite best standard of care
- Wounds with probe to bone were included



Articles

LeucoPatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked, randomised controlled trial

Frances Game, William Jeffcoate, Lise Tarnow, Judith L Jacobsen, Diane J Whitham, Eleanor F Harrison, Sharon J Ellender, Deborah Fitzsimmons, Magnus Löndahl, for the LeucoPatch II trial team

Summary

Background The LeucoPatch device uses bedside centrifugation without additional reagents to generate a disc comprising autologous leucocytes, platelets, and fibrin, which is applied to the surface of the wound. We aimed to test the effectiveness of LeucoPatch on the healing of hard-to-heal foot ulcers in people with diabetes.

Methods This was a multicentre, international, observer-masked, randomised controlled trial of people with diabetes and a hard-to-heal foot ulcer done in 32 specialist diabetic foot clinics in three countries (UK, Denmark, and Sweden). After a 4-week run-in period, those with a reduction in ulcer area of less than 50% were randomly allocated (1:1) by computer-generated, web-based randomisation (block sizes of two, four, and six) to either prespecified good standard care alone or care plus weekly application of LeucoPatch. The primary outcome was the proportion of ulcers that healed within 20 weeks assessed in the intention-to-treat population (all participants with post-randomisation data collected), defined as complete epithelialisation (confirmed by an observer who was masked to randomisation group), and remained healed for 4 weeks. This trial is registered with the ISRCTN registry, number 27665670, and ClinicalTrials.gov, number NCT02224742.

Lancet Diabetes Endocrinol 2018

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September 19, 2018
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See Online/Comment
http://dx.doi.org/10.1016/S2213-8587(18)30262-6

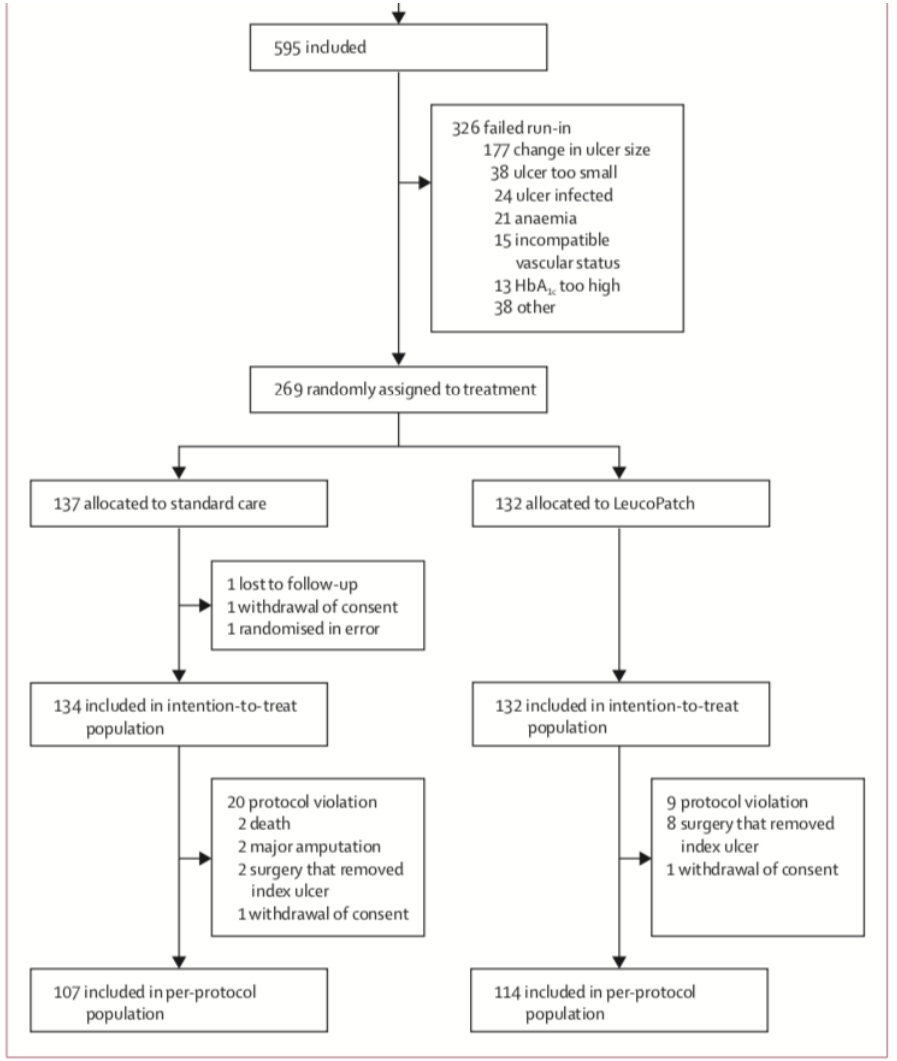
Department of Diabetes and Endocrinology, Derby Teaching Hospitals NHS Foundation Trust, Derby, UK (Prof F Game FRCP);
Department of Diabetes and Endocrinology, Nottingham University Hospitals Trust

*3C Patch previously known as LeucoPatch

Trial Profile

- 32 multidisciplinary centres in UK, Denmark, and Sweden

- HARD-TO-HEAL DIABETIC FOOT ULCERS
  - 595 consented patients
  - 326 excluded during run-in
    - 177 healed >50% in 4 wks
  - 269 patients randomised
  - 266 patients initiated treatment and were included in final analyses



Results: Well Matched Patient Populations

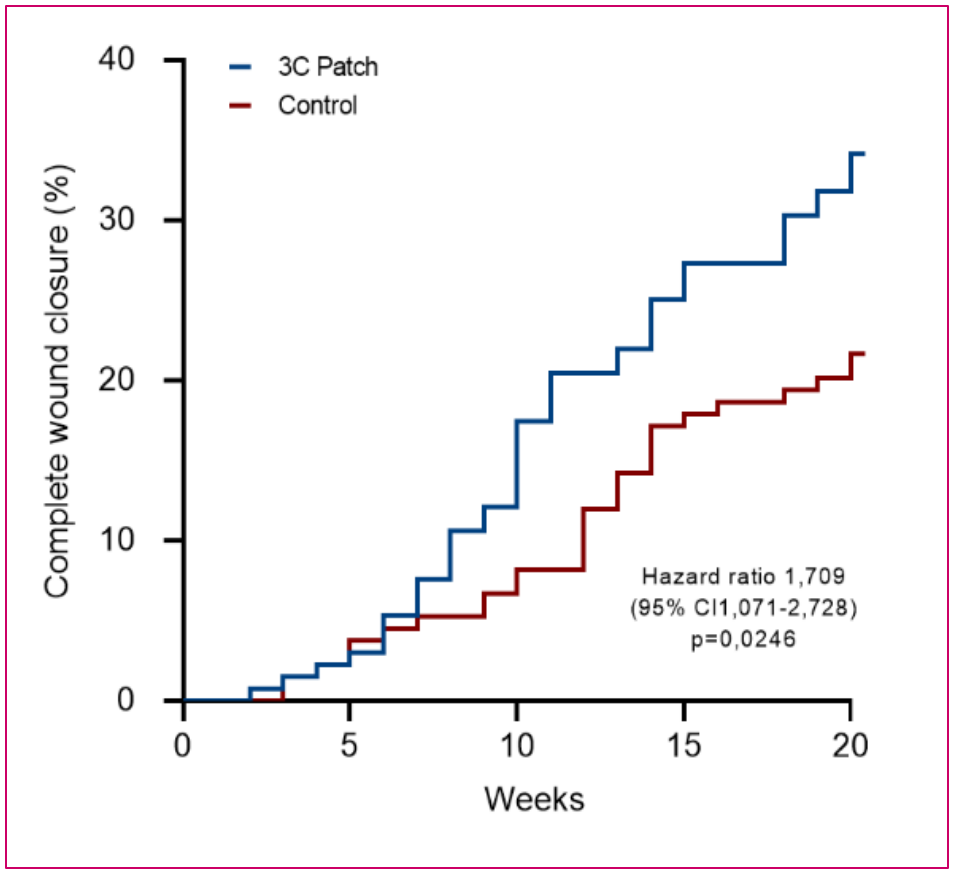
	Standard care (n=134)	LeucoPatch plus standard care (n=132)	Total (n=266)
General			
Mean age, years (SD)	62·0 (11·9)	61·9 (11·4)	61·9 (11·6)
Sex, n (%)			
Male	110 (82%)	107 (81%)	217 (82%)
Female	24 (18%)	25 (19%)	49 (18%)
Type 2 diabetes, n (%)	110 (82%)	112 (85%)	222 (83%)
Median duration of diabetes, years (IQR)	15 (8–22)	16 (10–25)	16 (10–23)
Diabetes-related complications, n (%)			
Cerebrovascular	17 (13%)	13 (10%)	30 (11%)
Cardiovascular	57 (43%)	55 (42%)	112 (42%)
Nephropathy	42 (31%)	48 (36%)	90 (34%)
Retinopathy	87 (65%)	87 (66%)	174 (65%)
Median HbA_{1c}, % (IQR)	8·2% (7·1–9·0)*	8·3% (7·2–9·2)†	8·2% (7·2–9·2)‡
Mean baseline haemoglobin, g/L (SD)	131 (15·4)	132 (15·6)	131 (15·5)
Estimated GFR, n (%)			
20–30 mL/min per 1·73 m²	3 (2%)	9 (7%)	12 (5%)
31–45 mL/min per 1·73 m²	15 (11%)	19 (14%)	34 (13%)
46–60 mL/min per 1·73 m²	34 (25%)	35 (27%)	69 (26%)
>60 mL/min per 1·73 m²	82 (61%)	69 (52%)	151 (57%)
Foot ulcer-related complications			
ABPI, n (%)			
0·5–0·79	16 (12%)	14 (11%)	30 (11%)
0·8–0·99	23 (17%)	30 (23%)	53 (20%)
1·0–1·4	73 (55%)	65 (49%)	138 (52%)
>1·4	22 (16%)	23 (17%)	45 (17%)
Loss of sensation at two or more sites, n (%)	117 (87%)	110 (83%)	227 (85%)

	Standard care (n=134)	LeucoPatch plus standard care (n=132)	Total (n=266)
Area of ulcer, n (%)			
≤100 mm²	34 (25%)	34 (26%)	68 (26%)
>100 mm²	100 (75%)	98 (74%)	198 (74%)
Mean area of ulcer, mm² (SD)	252·7 (226·5)	228·8 (207·43)	240·8 (217·16)
Depth of ulcer, n (%)			
Superficial	120 (90%)	110 (83%)	230 (87%)
Down to tendon	11 (8%)	16 (12%)	27 (10%)
Down to bone	3 (2%)	6 (5%)	9 (3%)
Affected foot position, n (%)§			
Total forefoot	99 (74%)	108 (82%)	207 (78%)
Plantar forefoot	54 (40%)	57 (43%)	111 (42%)
Hind foot	35 (26%)	24 (18%)	59 (22%)
Type of offloading			
Bedbound or immobile	3 (2%)	4 (3%)	7 (3%)
Normal footwear	10 (7%)	14 (11%)	24 (9%)
Normal footwear plus fitted insoles or inserts	6 (4%)	6 (5%)	12 (5%)
Fitted footwear or orthoses	35 (26%)	38 (29%)	73 (27%)
Padded slipper or shoe	27 (20%)	28 (21%)	55 (21%)
Removable cast or device for foot	34 (25%)	31 (23%)	65 (24%)
Removable cast or device for lower leg	25 (19%)	17 (13%)	42 (16%)
Non-removable cast or device for foot	1 (1%)	3 (2%)	4 (2%)
Non-removable cast or device for lower leg	4 (3%)	6 (5%)	10 (4%)

Data are given as median (IQR) or number of participants (%), unless otherwise stated. Percentages might not sum to 100% because of rounding. GFR=glomerular filtration rate. ABPI=ankle brachial pressure index. *66 mmol/mol (IQR 54–75). †62 mmol/mol (IQR 55–77). ‡66 mmol/mol (IQR 55–77). §Forefoot was defined as distal to and hind foot as proximal to the tarsometatarsal joint.

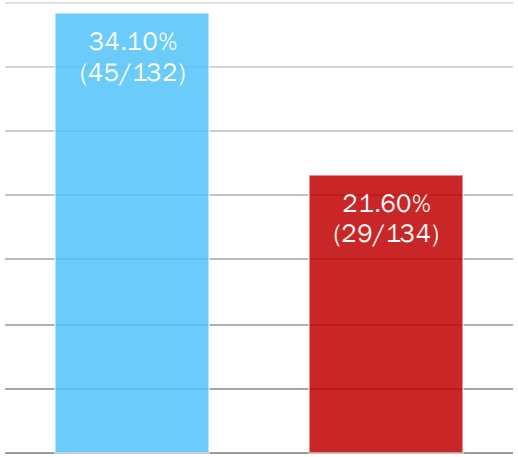
Table 1: Baseline clinical characteristics

Autologous MLPF Patch Improves Healing Of Hard-to-Heal Diabetic Foot Ulcers



Odds ratio 1.58

(CI: 1.06-2.35)



Adjusted odds ratio, as per protocol:

1.9 (CI: 1.09-3.31)

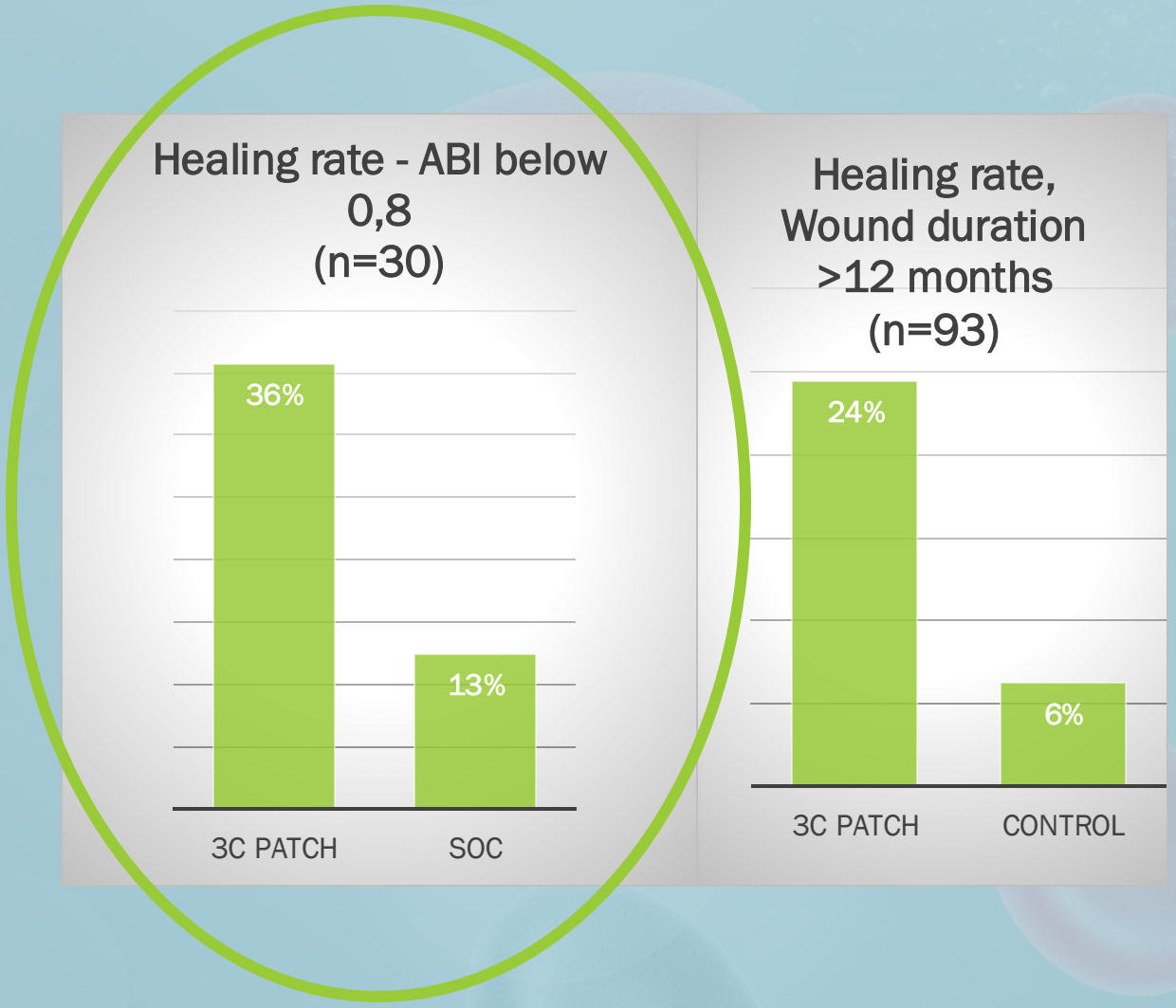
Large International RCT

- Autologous MLPF patch demonstrated a significantly higher incidence of healing within 20 wks in very hard-to-heal ulcers.
- Time to complete healing was significantly shorter 72 vs 84 days
- The 3C Patch RCT is more inclusive than other trials – and select harder to heal wounds; why it is more relevant for the population that challenges clinics.

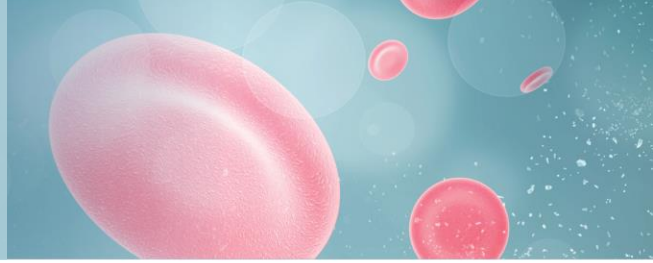
Game F., Jeffcoate W., ..., Löndahl M., LeucoPatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked randomized controlled trial. Lancet Diabetes Endocrinol. 2018 Nov;6(11):870-878.

Relevant Patient Population, Interesting Subgroup Data

- Non-responding for 4 wks
- Grade 3 wounds included
- ABPI down to 0.5
- “Real” wound care patients from >30 centers
- Best standard of care, including debridement, offloading, NPWT, protease inhibitors, etc.
- Control group continued treatment with optimal care



Real World Data Publication, Mendivil, et al. 2023



Original Investigation [OPEN]

Retrospective Data Analysis of the Use of an Autologous Multilayered Leukocyte, Platelet, and Fibrin Patch for Diabetic Foot Ulcers Treatment in Daily Clinical Practice

Jason M. Mendivil, DPM; Lorena C. Henderson, APRN, MSN, FNP-C; Orion S. Olivas; Mia A. Deanda; and Martin L. Johnson, MD, MPH, FACS

ABSTRACT

OBJECTIVE: To describe the healing outcome of chronic, hard-to-heal diabetic foot ulcers (DFUs) treated with an autologous multilayered leukocyte, platelet, and fibrin (MLPF) patch in addition to the best standard of care, in a real-world clinical setting of two US amputation preventive centers.

METHODS: In this retrospective study of patients treated between September 2021 and October 2022, the authors analyzed DFU healing outcomes based on Wound, Ischemia, and foot Infection-derived amputation risk.

RESULTS: All 36 patients had a diagnosis of type 2 diabetes and 29 (81%) were male. Their average age was 61.4 years, body mass index was 29.2 kg/m^2, and glycated hemoglobin was 7.9. Twenty-seven patients (78%) were diagnosed with peripheral vascular disease, 20 (56%) underwent a peripheral vascular procedure, 15 (42%) had a prior amputation, and 6 (17%) were on hemodialysis. Average wound size was 4.9 cm^2, and wound age was 9.5 months. Twelve patients (32%) were classified as low risk, 15 (39%) as moderate risk, and 11 (29%) as high risk for amputation. Within 12 weeks of the first MLPF patch application, nine wounds (24%) healed. After 20 weeks, 23 wounds (61%) were closed, and by follow-up, 30 wounds (79%) healed. No amputations were noted. Compared with published data, 40% fewer patients underwent readmission within 30 days, with 72% shorter admission duration.

CONCLUSIONS: Real-world clinical experiences using the MLPF patch to treat hard-to-heal DFUs resulted in the majority of wounds healing. Few patients experienced a readmission within 30 days, and the average admission duration was short.

INTRODUCTION

In patients with diabetes mellitus, diabetic foot ulcers (DFUs) are the fastest-growing chronic complication with an annual incidence of 2.4% to 2.6% and prevalence of 4% to 10% worldwide.[1] Even after a DFU has healed, recurrence is common: Approximately 40% of patients have a recurrence within the first year after ulcer healing, almost 60% within 3 years, and 65% within 5 years.[2] Management of patients with DFUs follows a holistic approach, with standard-of-care treatments including regular debridement, offloading, metabolic control, treatment of comorbidities, local ulcer care, regular foot care, and vascular assessment. Despite improved outcomes following standard treatment, more than half of DFUs become infected, with approximately 20% of moderate or severe diabetic foot infections leading to some level of amputation.[2] Hicks et al[3] reported 30-day readmission rates of more than 20% for patients with DFUs with an average inpatient stay of 9 days, resulting in more than double the cost of care per patient from US $28,977 to US $79,315.[3]

In addition to standard practice in DFU care, a range

Table 1. PATIENT DEMOGRAPHICS AND CHARACTERISTICS AT BASELINE (N = 36)

Variable	Mean (Range) or n (%)
Age, y	62.5 (36–89)
Sex, male	29 (81)
Diabetes type II	36 (100)
Body mass index, kg/m^2	27.5 (19.4–49.5)
HbA_{1c}, n = 18	7.9 (5.6–10.6)
CKD	9 (25)
Dialysis	6 (17)
Neuropathy	31 (86)
PVD	28 (78)
Prior revascularization	20 (56)
Prior amputation	15 (42)

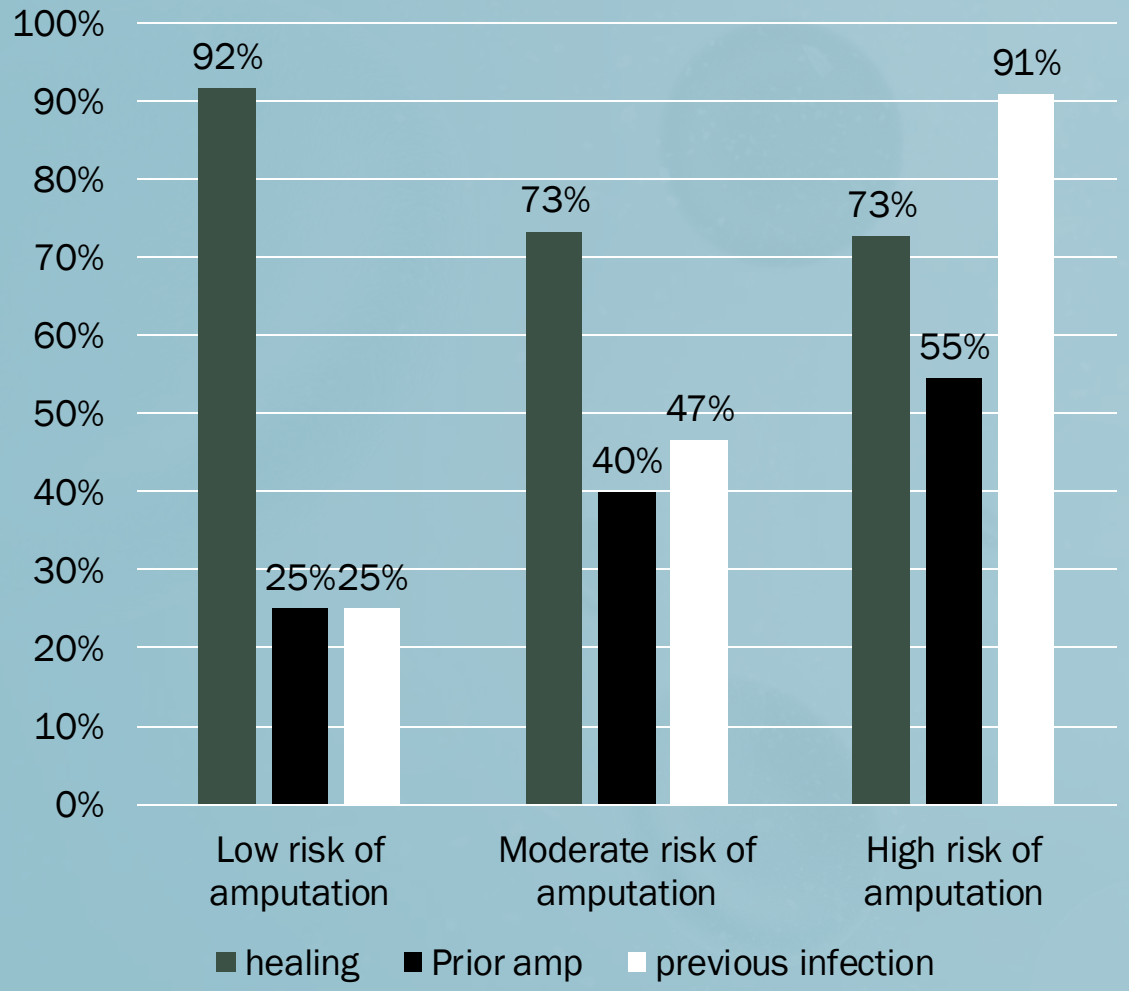
Abbreviations: CKD, chronic kidney disease; HbA_{1c}, glycated hemoglobin; PVD, peripheral vascular disease.

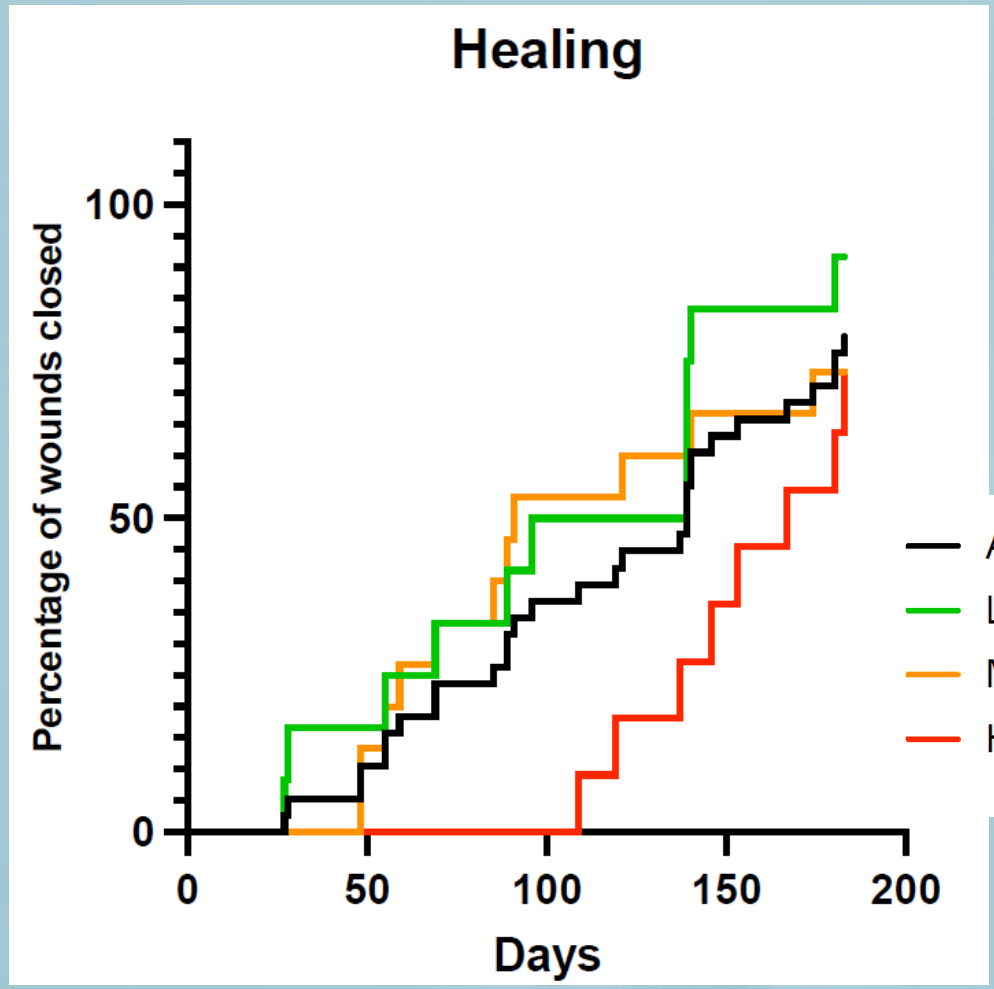
Table 2. WOUND CHARACTERISTICS AT START OF MLPF PATCH TREATMENT (N = 38)

Characteristics	Mean (Range) or n (%)
Wound size, cm^2	4.9 (0.12–39)
Wound age, mo	9.5 (1–60)
Wagner wound grade	
1	3 (8)
2	33 (89)
3	1 (3)
WIfI classification-based risk for amputation	
Low	12 (32)
Moderate	15 (39)
High	11 (29)
Wound locations	
Plantar foot	15 (39)
Toe	5 (13)
Transmetatarsal amputation	5 (13)
Lateral foot	5 (13)
Lower leg	6 (16)
Heel	2 (5)

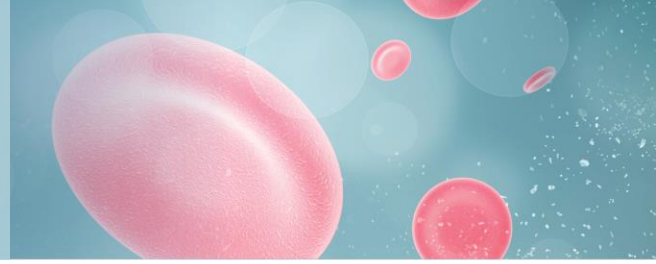
Abbreviations: MLPF, multilayered leukocyte, platelet, and fibrin; WIfI, Wound, Ischemia, and foot Infection.

Real World Data Publication, Mendivil, et al. 2023





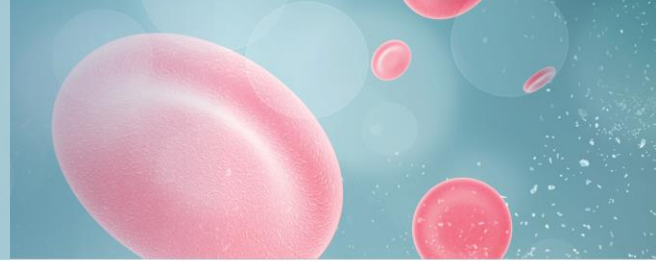
Real World Evidence:
St. Vincent Hospital, Worcester, MA



- Use of autologous MLPF patch at St. Vincent's has resulted in healing in patients who have failed other advanced modalities, such as:
  - Hyperbaric Oxygen Therapy (HBOT)
  - Cellular Tissue Products (CTPs)
  - Surgical Repair

- The ease of use of the autologous MLPF patch system and the patient engagement has been integral in our success

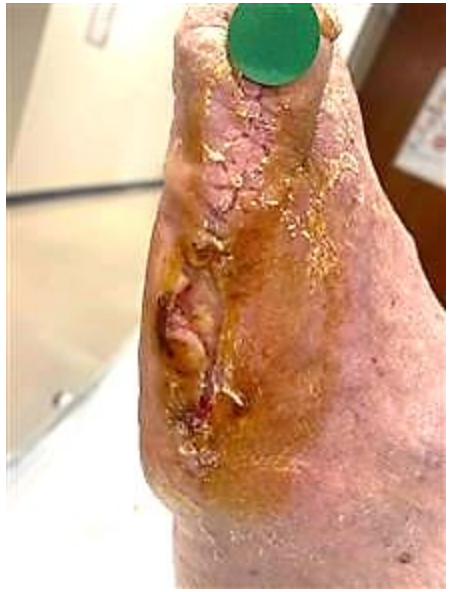
Real World Evidence: SVH, Worcester, MA



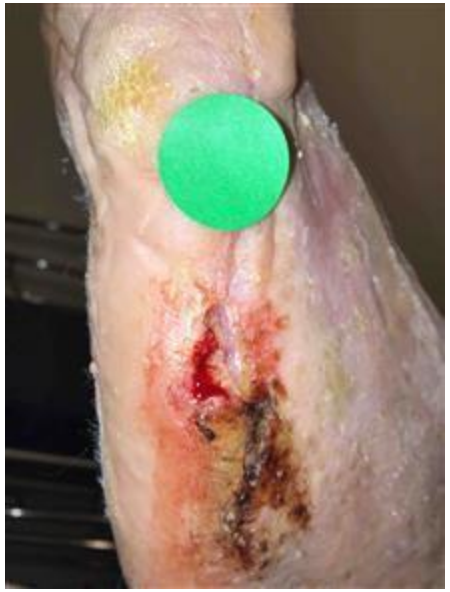
- 81y Male
  - Treated in our clinic for over 9 months.
  - History of osteomyelitis, receiving HBOT for 3 mos
  - Had also failed CTP applications and attempts at surgical closure
  - After just 6 applications of the autologous MLPF patch, in conjunction with the use of NIRS, his wound went from 5.3cm^2 to healed.
  - Patient went from feeling he had little hope of healing to experiencing a new lease on life

Real World Evidence:
SVH, Worcester, MA

81y Male

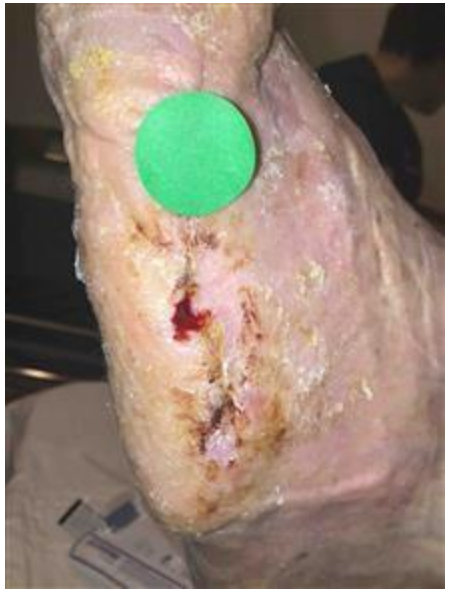


8/8/24



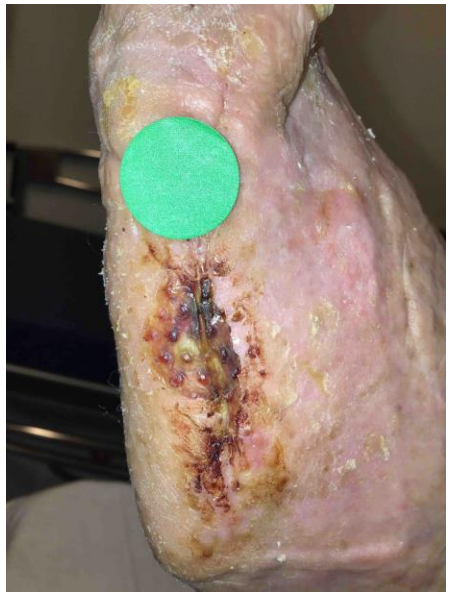
8/28/24

1.2x0.7x0.2cm



9/19/24

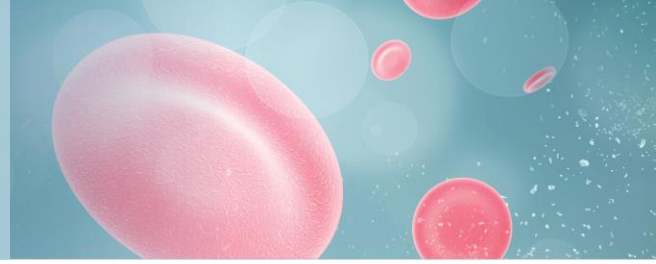
0.6x.05x0.1cm



9/26/24

Fully Closed

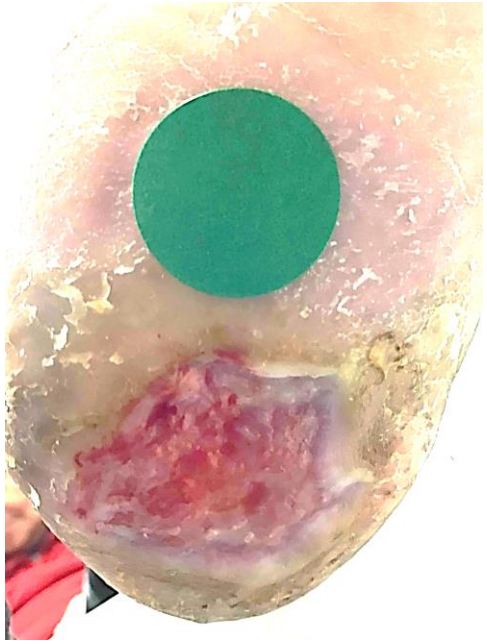
Real World Evidence: SVH, Worcester, MA

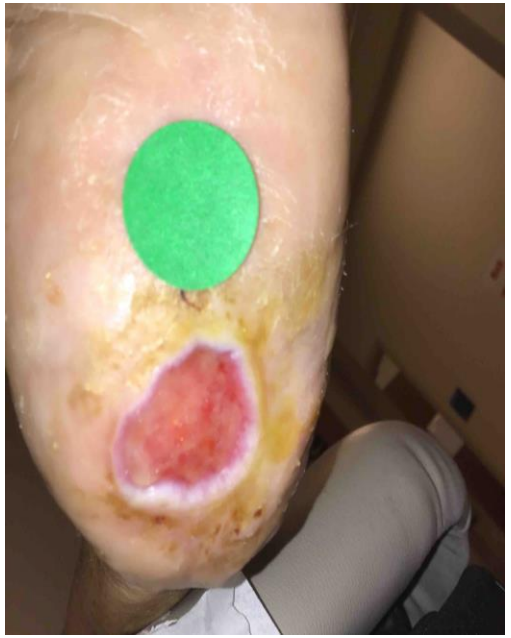


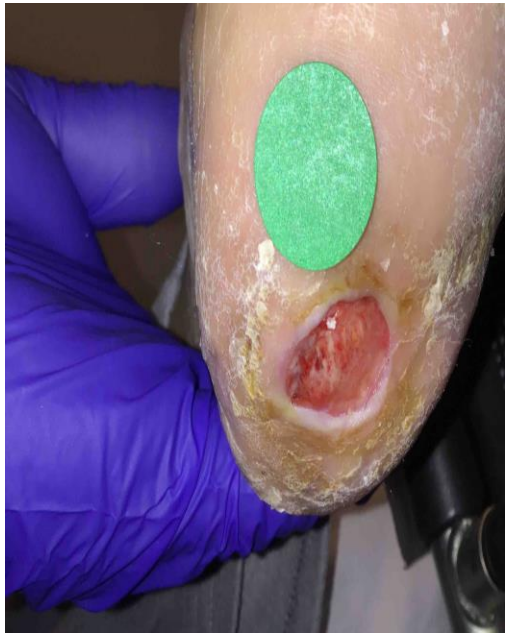
- 82y Female
- Wound present for over 1 yr
- Prior therapies tried: HBOT 12/12/23 - 3/5/2024; Skin sub 6/4/2024 - 10/8/2024; also had I&D once and revascularization in 2024. Everything failed to close wound
- Initial measurements: on 10/15/2024, first day of autologous MLPF patch application 1.75 x 2.27 x 0.2cm
- Measurements at halfway point: 1/7/2025, 0.95 x 1.45 x 0.1
- Current measurements : 0.45 x 0.89 - 0.1cm

Real World Evidence:
SVH, Worcester, MA

82y Female







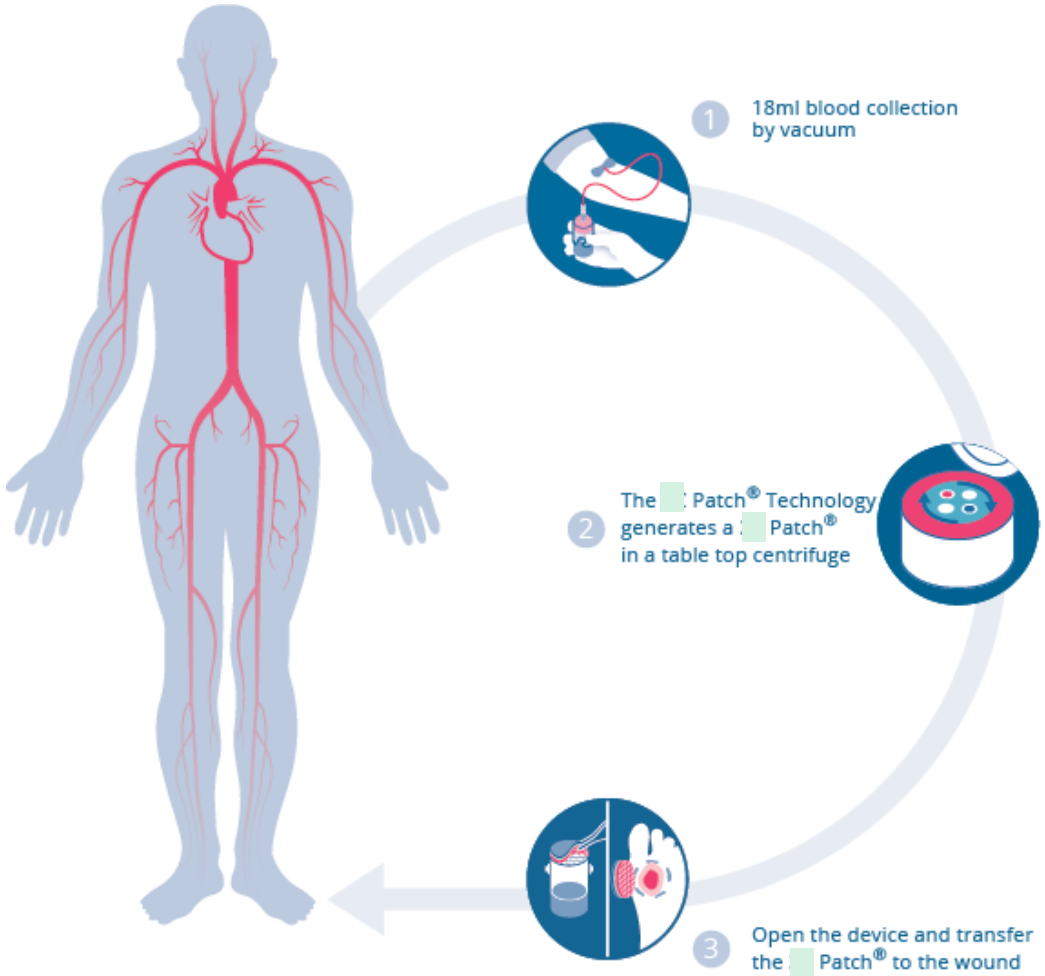
Conclusion

- The use of the autologous patch has demonstrated improved outcomes and healing in the difficult to treat diabetic ulcer population, even in patients with low ABIs
- The reason for this is the ability of the autologous MLPF patch to improve angiogenesis, thus improving the perfusion to these wounds
- We now consider the use of the autologous MLPF patch on patients as an initial treatment, rather than a last resort

Clinic Workflow and Autologous MLPF Patch Process

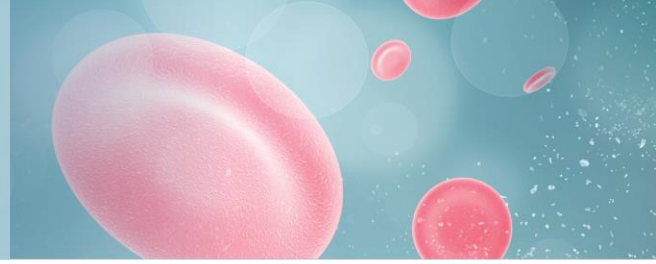
James Y. Lin, DO, MS (MedEd), MHSA
LECOM Institute for Advanced Wound Care & Hyperbaric Medicine
Erie, PA

Clinic Workflow & Autologous Multilayered Leukocyte, Platelet, and Fibrin (MLPF) Patch Process



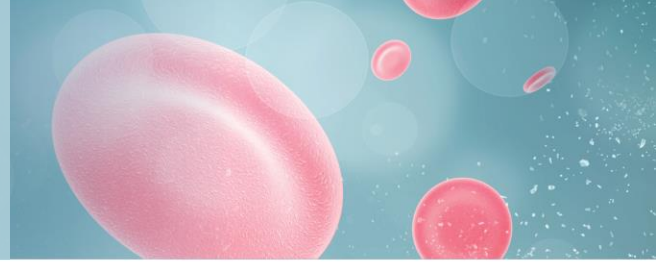
A simple, point-of-care solution, based on the automated, fully integrated MLPF System.

Clinical Workflow Impact



- Many facilities worry about the impact of an autologous product on their workflow
- “It will slow down our very busy clinic”
- “Our nurses don’t have time to draw blood” OR “Our nurses haven’t drawn blood in years!”
- “We don’t have the space for the equipment”

Clinical Workflow Can Actually Improve!



- Reduction in average healing time
- Fewer clinic visits per patients
- Lower readmission or complication rates
- Higher patient satisfaction scores
- Increase in patient intake due to better throughput and outcomes

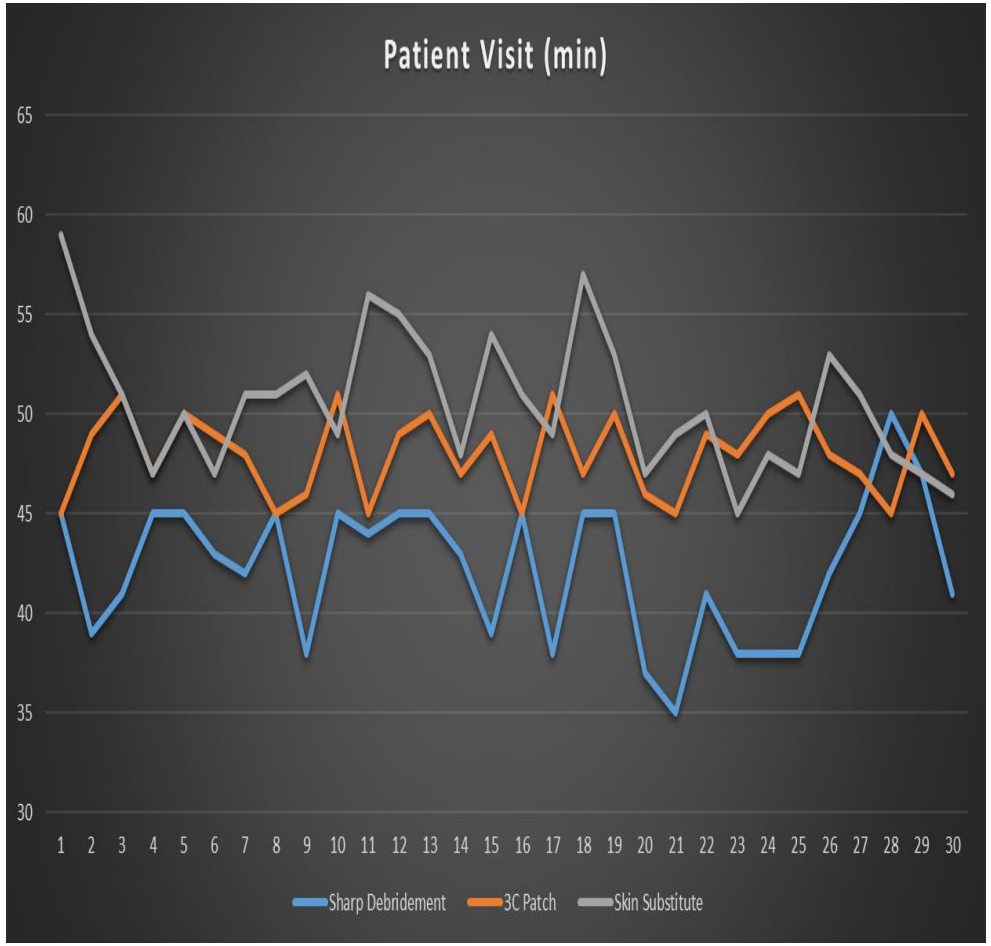
Recent Research to Support Use of MLPF Patch

- A study done in my clinic demonstrated that the use of the MLPF Patch took less time than the application of a Cellular Tissue Product(CTP)
  - We compared just debridement vs debridement with the MLPF Patch vs debridement with a CTP
  - This data is only representative of an outpatient wound care center

- After analyzing the data statistics (Students' T-test), we found a statistically significant difference between the pairs with a 95% CI:

Procedure	Average Time(minutes)
Sharp debridement only	42.3
Sharp debridement + 3C Patch	48.0
Sharp debridement + Cellular Tissue Product	50.6

Recent Research to Support Use of MLPF Patch



Recent Research to Support Use of MLPF Patch

- Another retrospective study done by Mendivil et al. performed in 2 limb salvage clinics in the US looked at MLPF patch real world outcomes in chronic DFUs when used adjunctively to SOC. (9/21-10/22)
  - Found that not only were there no amputations in the MLPF Patch patients but also:
  - Only 5 of 36 patients (13.9%) were readmitted to the hospital in the first 30 days with a total of 8 admissions (1.6 per patient). Average length of stay was 2.5 days
  - Compared to Hicks' study(2019) that described 30-day readmission rates of more than 20%(23.2%) for DFU patients with an average length of stay of 9 days
  - Conclusion: 50% fewer patients underwent readmission within 30 days (13.9% vs. 23.2%), with 72% shorter admission duration (average length of stay 2.5 vs. 9.0 days) with the use of the MLPF patch

Key Performance Indicators

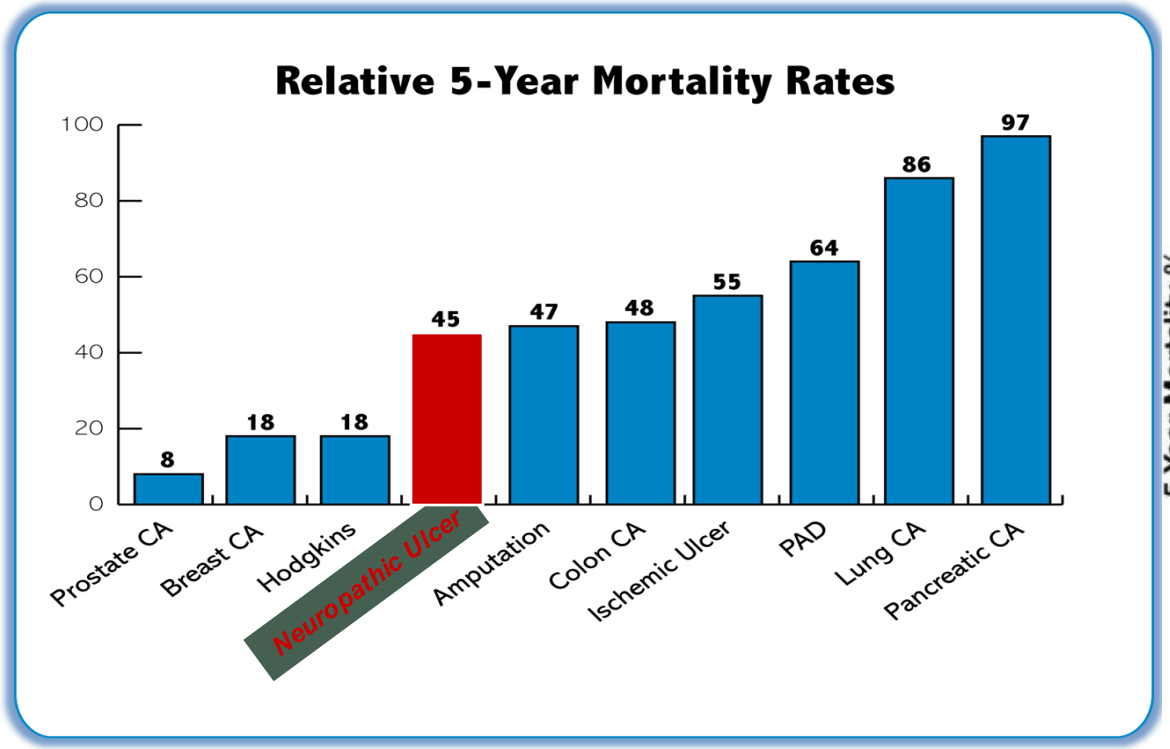
Key Performance Indicators
Typical Facility Goal(s)

Distinction and Excellence

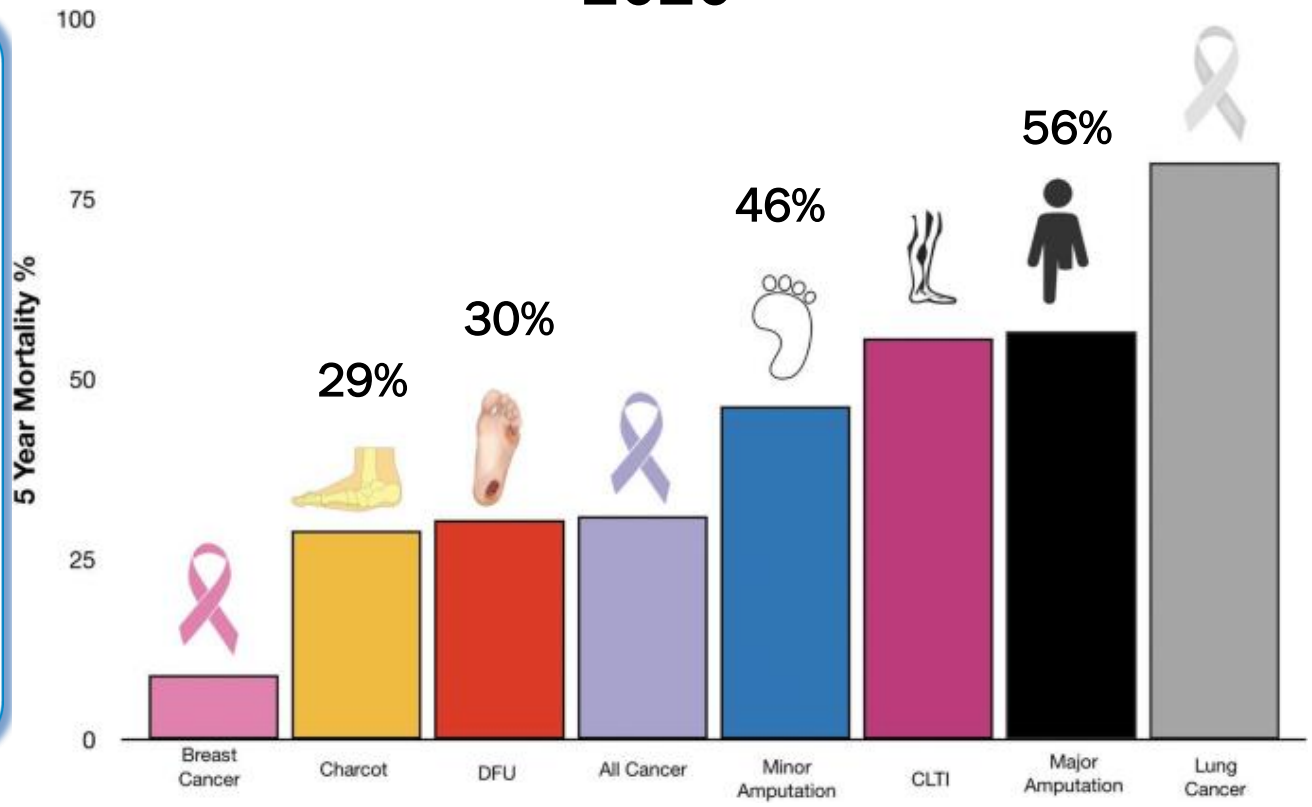
- Healing Rate
- Median Days to Heal
- Outliers
- Patient Satisfaction

Consequences of Unhealed Neuropathic Ulcers

2007



2020



- Nearly half of all unhealed neuropathic ulcers result in death within 5 yrs

- Armstrong, D.G., Swerdlow, M.A., Armstrong, A.A. et al. Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. J Foot Ankle Res 13, 16 (2020). https://doi.org/10.1186/s13047-020-00383-2

Armstrong DG. *Int Wound J*. 2007;4(4):286-287.

- Diabetic Foot Ulcerations, a 50% decrease of the wound area at 4 wks has been found to be a strong predictor of wound healing at 12 wks (Patry J, et al. 2021)

Standard Wound Care 4 wks

50% Reduction?

Yes

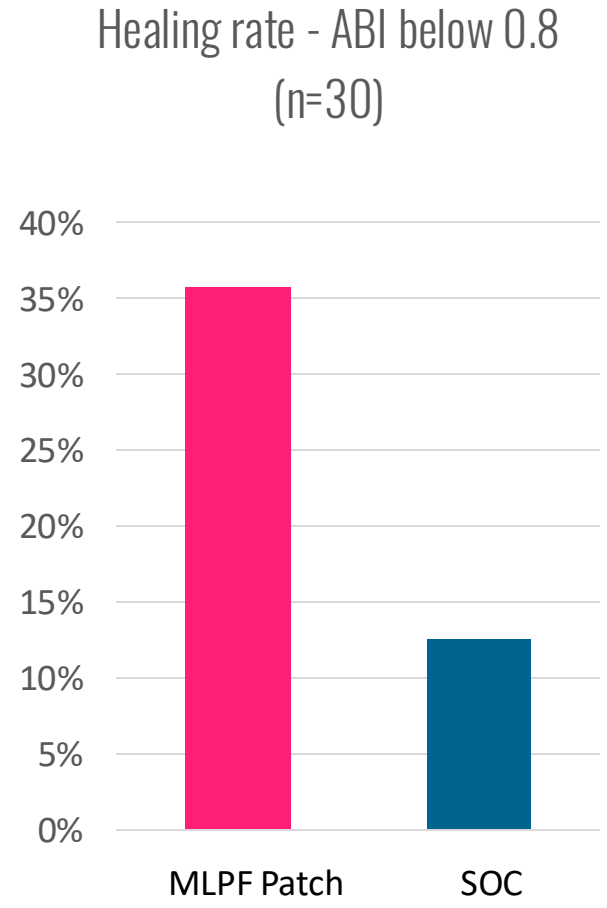
Continue with Treatment

No

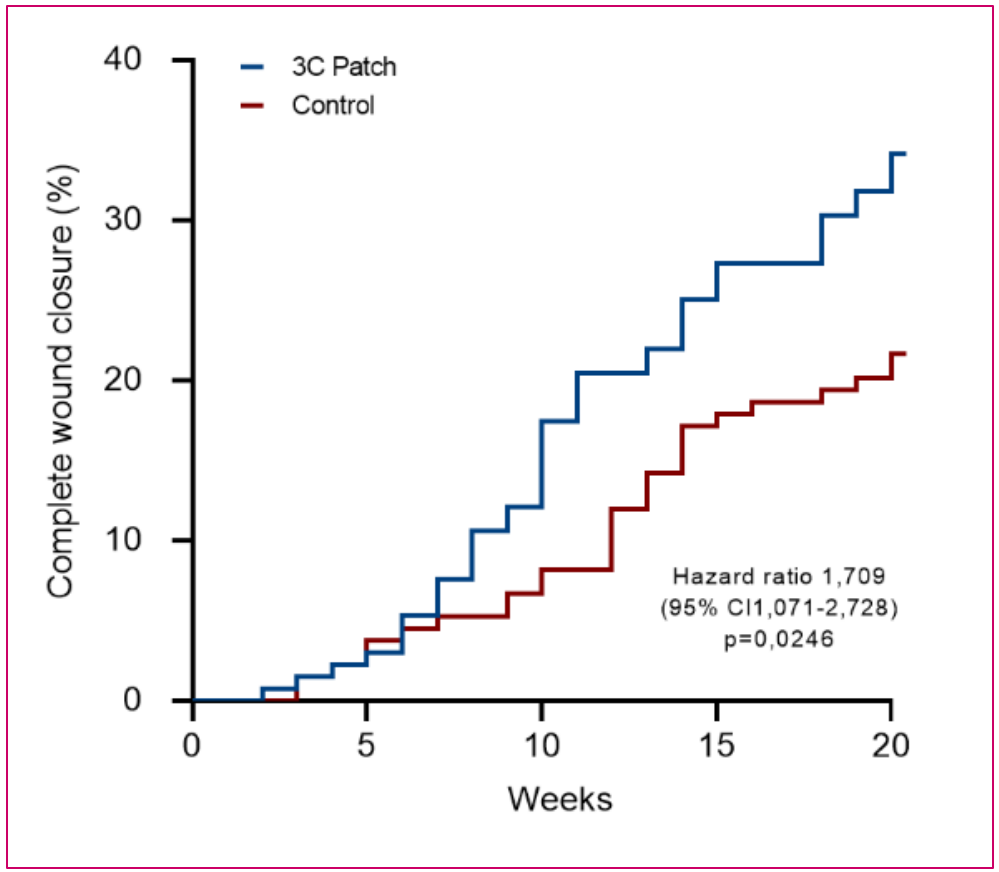
Use Advanced Modality

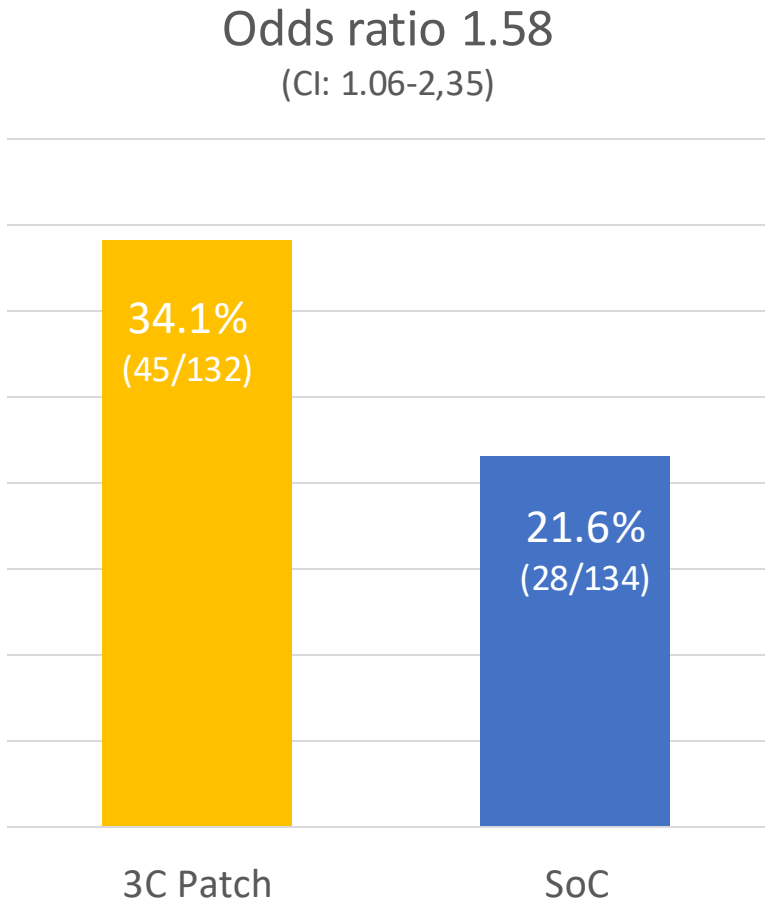
Relevant Patient Population

- Robust RCT that was published in *Lancet* in 2018 included:
- Run-in period of 4 wks
- Wagner Grade 3 wounds
- ABI down to 0.5
- “Real” wound care patients from >30 centers
- Best standard of care including debridement, offloading, NPWT, protease inhibitors, etc.



MLPF Patch Improves Healing of Hard-to-Heal Diabetic Foot Ulcers

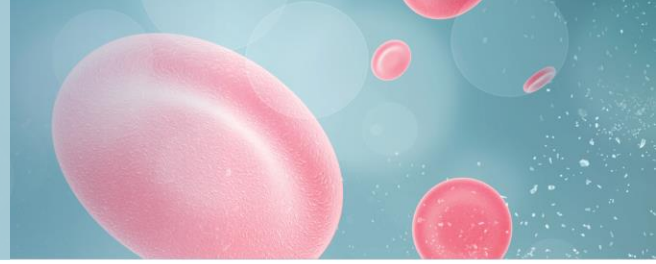




Adjusted odds ratio, as per protocol:

Clinic Workflow

Recommended Clinic Workflow



- Identify need of MLPF Patch for current visit (Initiate Intake)
  - For example, ulceration may be healed or need to address s/s of infection
- Draw blood by vacuum in the device (18 mL)
  - Prep supplies prior to visit (kit): blood draw needle, tourniquet, alcohol pad, cotton ball, adhesive bandage
  - Use vein finder to assist if needed
- Place the filled device in the automated centrifuge per manufacturer guidelines
  - No obstructive stickers
- Complete Intake and Provider visit (Assessment, Debridement, and Other Modalities)

—Normal visit takes place while blood sample is in centrifuge

—Approx. 18 minutes

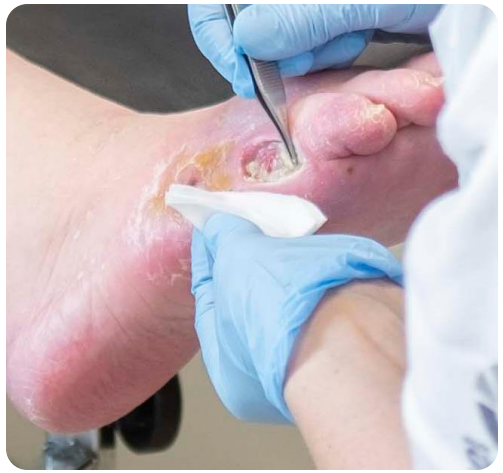
—Blood thinners may prolong spin time

- Collect MLPF Patch post centrifugation, coagulation, and compaction complete
- Transfer the MLPF Patch to the wound bed and bolster in place with wound contact layer
- Apply any needed secondary dressings or adjunct advanced modalities

MLPF Patch Procedure

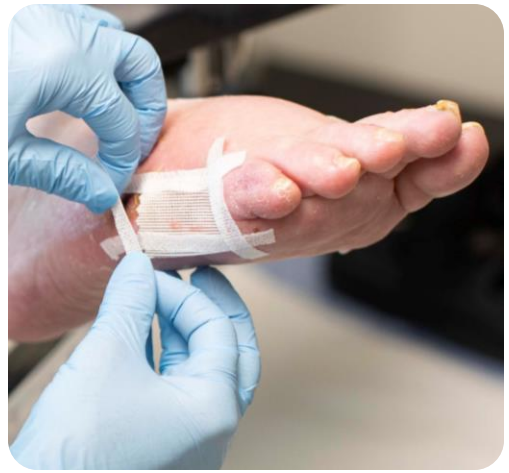
Draw blood

Place the device in the centrifuge



Clean and debride the wound

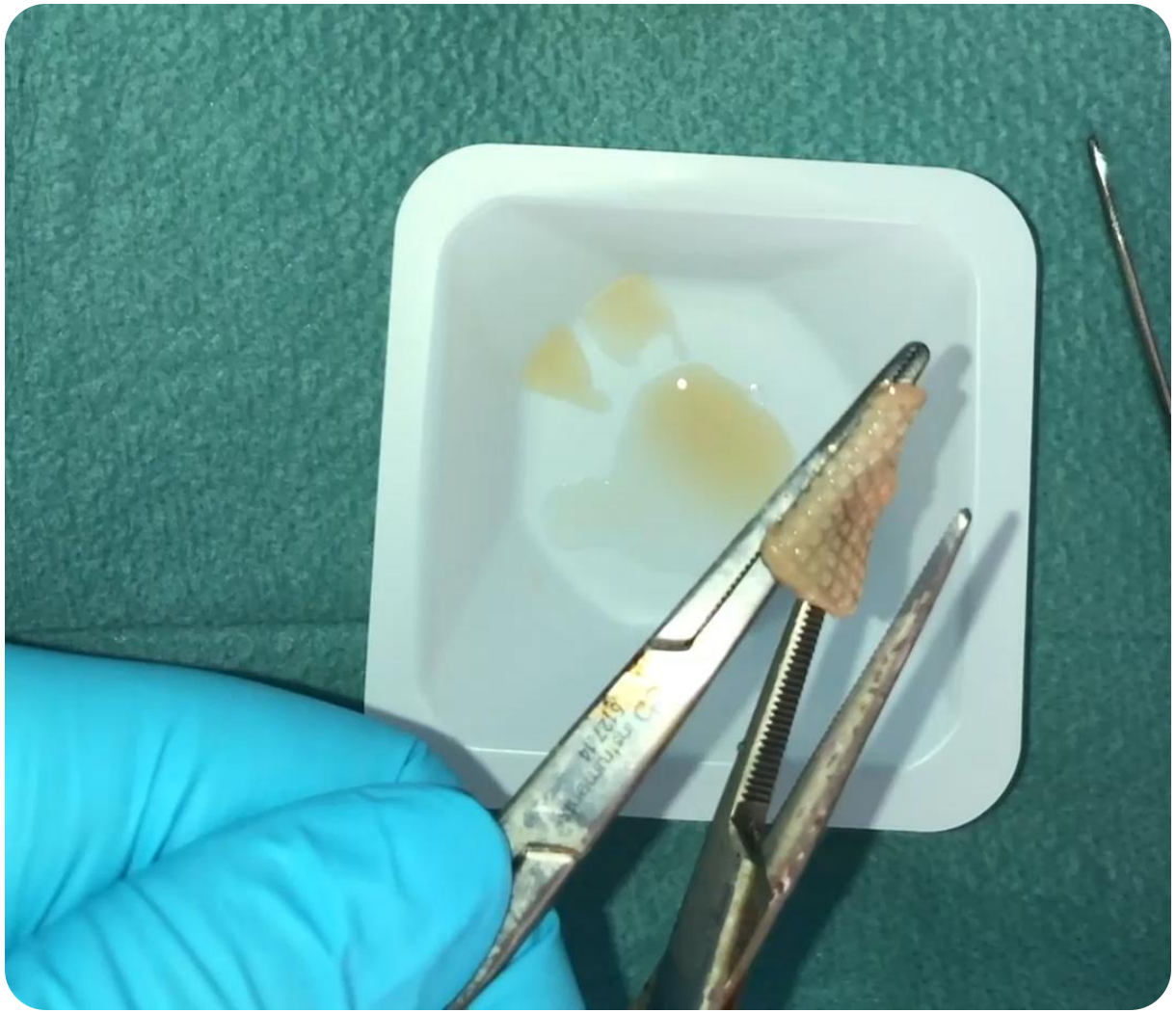
Remove the MLPF Patch from the device



Apply the MLPF Patch and dress the wound

MLPF Patch

The autologous fibrin provides strength and ease of handling



Factors that Improve Treatment Outcome

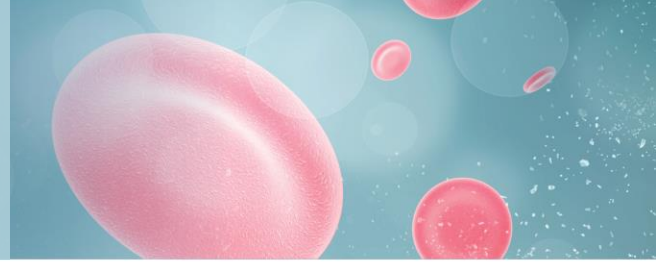
- The wound is debrided to bleeding before patch is applied
- Appropriate off-loading modalities are key
- Ensure adequate perfusion for wound healing
- Secondary dressing change frequency depends on exudate (typically decreases after a few weeks of treatment)
- Consider from week-to-week if MLPF Patch is effective

Patient and Staff Adoption of MLPF Patch

- **Implementing MLPF Patch**
  - Staff training
  - Space requirements
  - Patient scheduling
  - Patients allowed up to 20 wks of treatment
- **Clinical workflow as discussed earlier**
- **Patients' acceptance**
  - Well-adapted to receive weekly blood draws
  - Patient involvement and engagement in addition to wound improvement

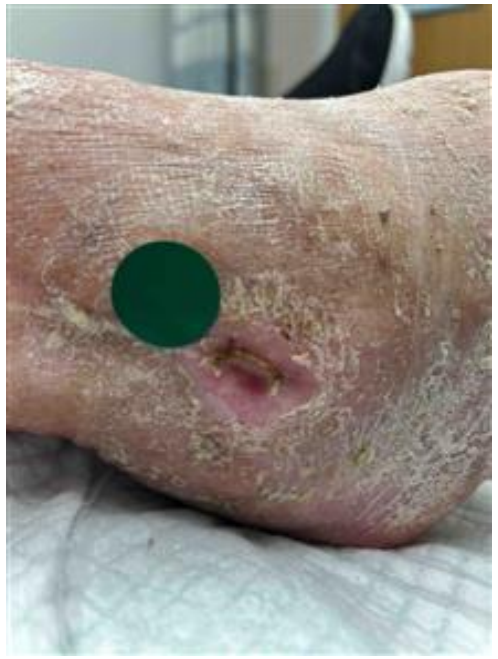
Case Studies

Patient #1-SS

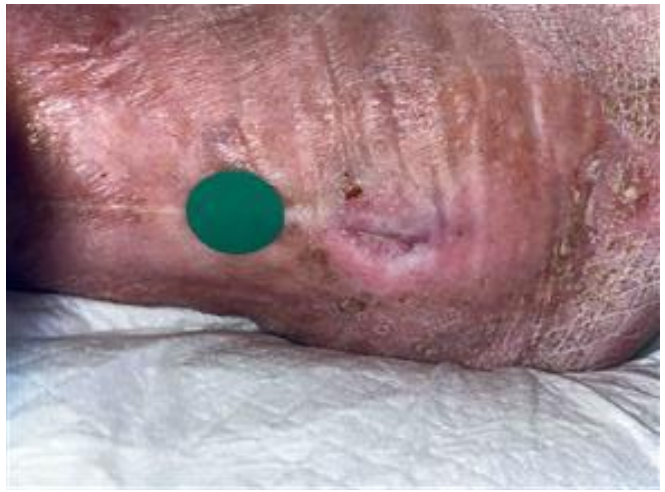


- 73 y/o female
- PMH: DM II, HTN, Hyperlipidemia, Chronic DVT RLE, Abdominal hernia surgery
- Venous Reflux: Positive – 9/30/24 Venous procedure
- Chronic diabetic ulceration to right lateral ankle with chronic edema.
  - Reoccurring ulceration despite medical grade compression during treatment and conventional post healing compression therapy.
- After 10 applications of the autologous MLPF patch, site remains closed and stable with no reoccurrence

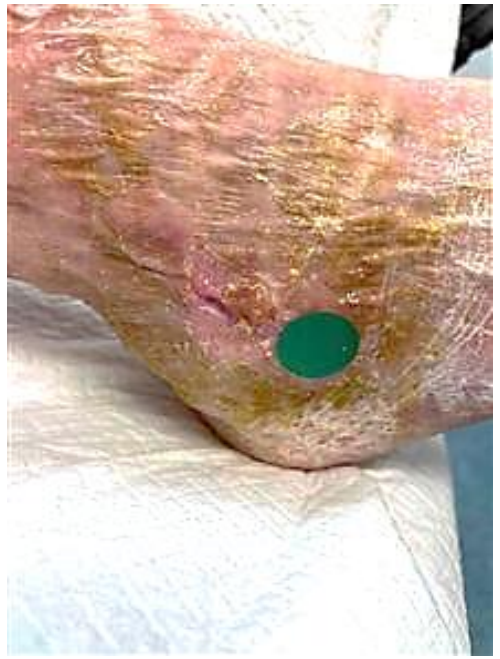
Patient #1-SS



9/16/24 #1

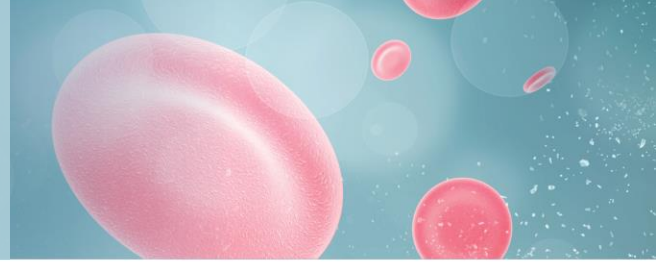


10/21/25 #5



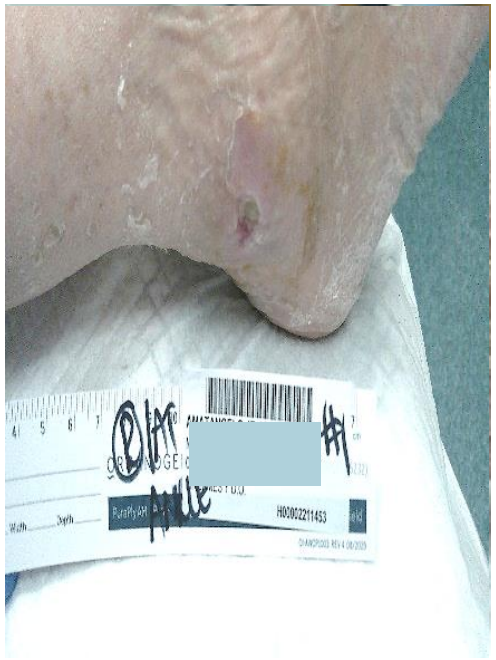
12/16/24 #9

Patient #2-JA

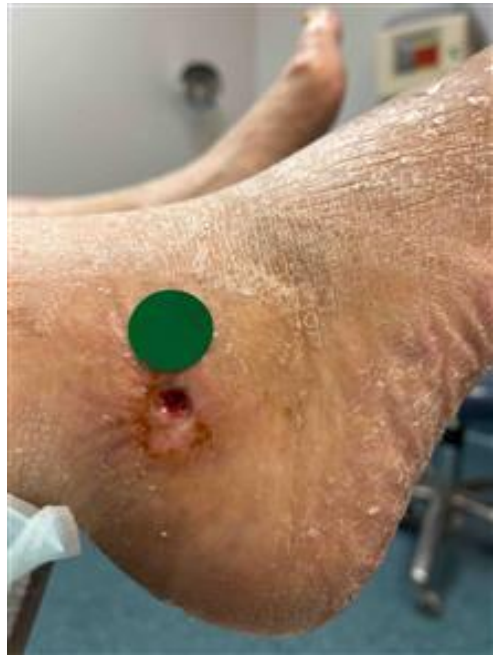


- 90 y/o male
- PMH: DM II, PAD, GERD, hyperlipidemia, CHF, amputation of right toe due to ischemia
- ABI: RLE 1.21
- Chronic diabetic ulceration to right lateral ankle.
  - Nonhealing over multiple months.
- Evaluated at our WCC for second opinion for wound healing.
- After 9 applications of the MLPF patch, site remained closed and stable with no reoccurrence

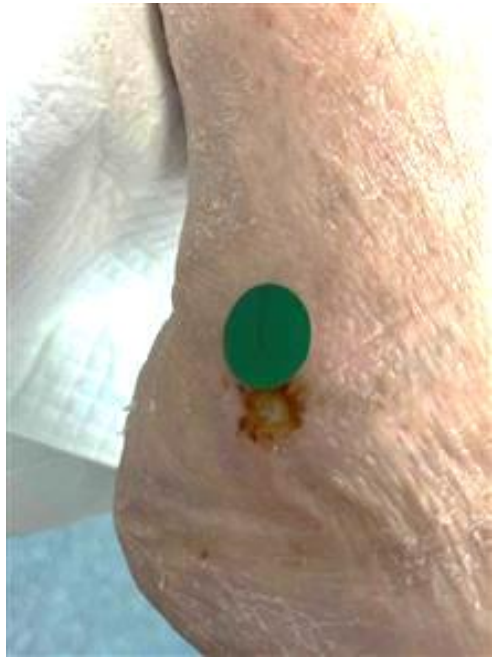
Patient #2-JA



07/02/24 #4 *



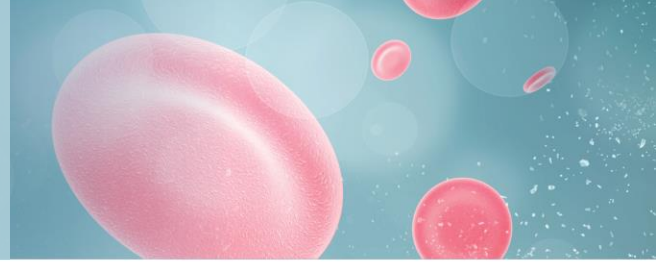
07/23/24 #7



08/06/24 #9

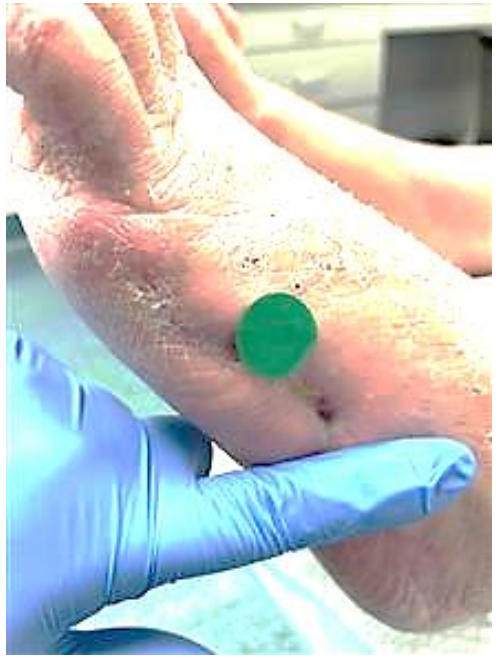
Switched to new EMR and pictures prior to this date were unavailable from old EMR

Patient #3-AC

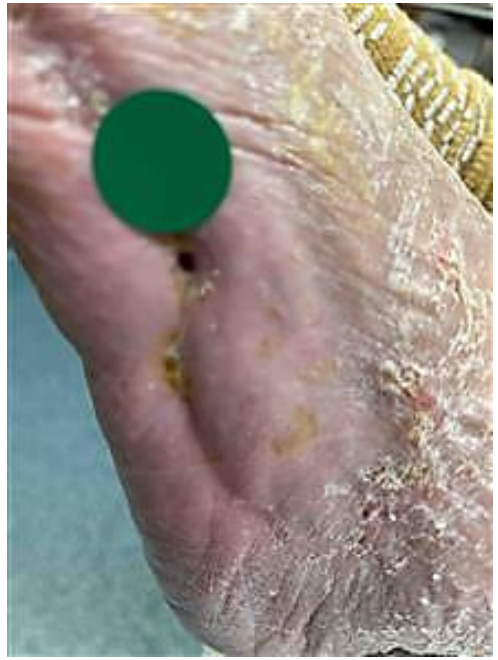


- 82 y/o male
- PMH: DM II, DVT LLE,
- Post-surgical amputation site of the left lateral 5th metatarsal due to osteomyelitis.
  - Noncompliant with diabetic management and offloading.
- Approximately 12 weeks post op due to nonhealing residual site, transitioned to wound care.
- After 4 applications of the MLPF patch, site remains closed and stable with no reoccurrence

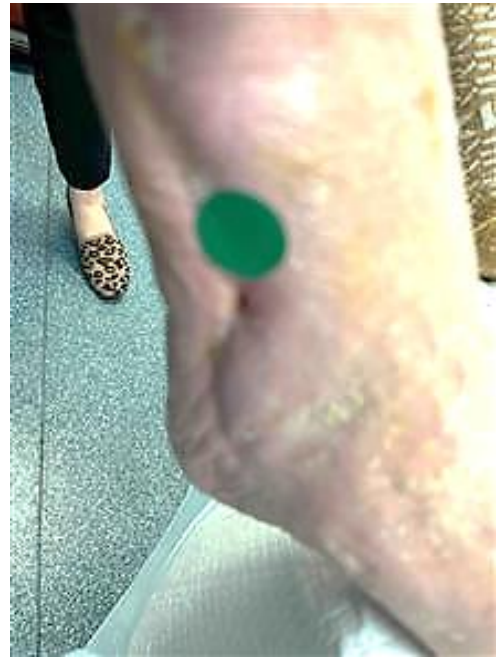
Patient #3-AC



12/6/24 #1

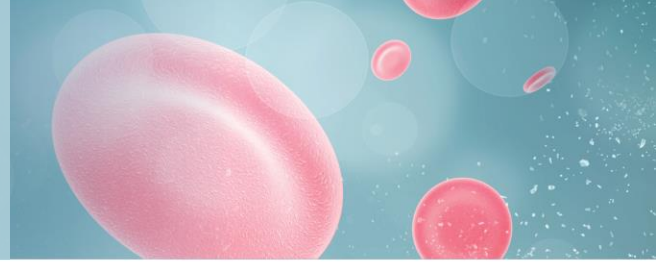


12/20/24
#3



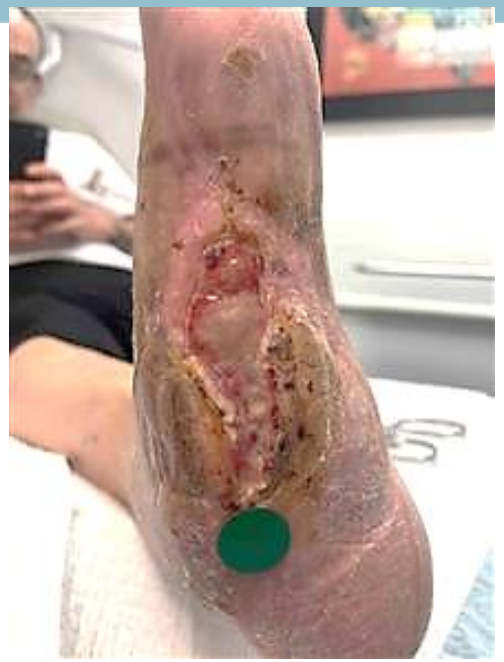
12/27/24 #4

Patient #4-JB

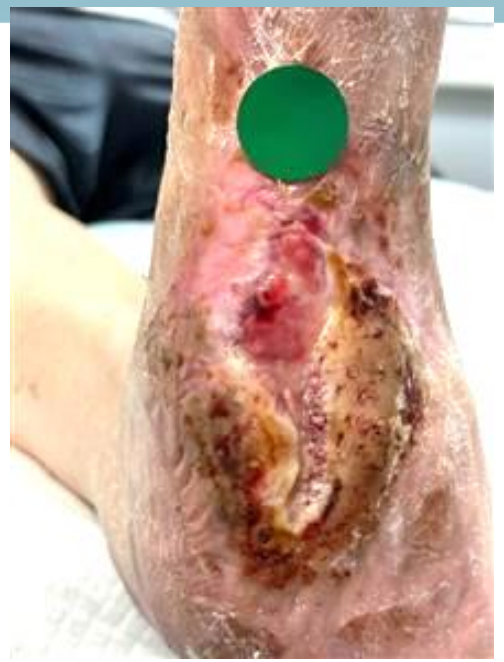


- 54 y/o male
- PMH: DM II, HTN, CAD, Neuropathy
- Post-surgical site due to osteomyelitis.
- After 4 wks of conservative post-surgical care, ulceration remains unhealed.
- After 10 applications of the MLPF patch, site remains closed and stable with no reoccurrence

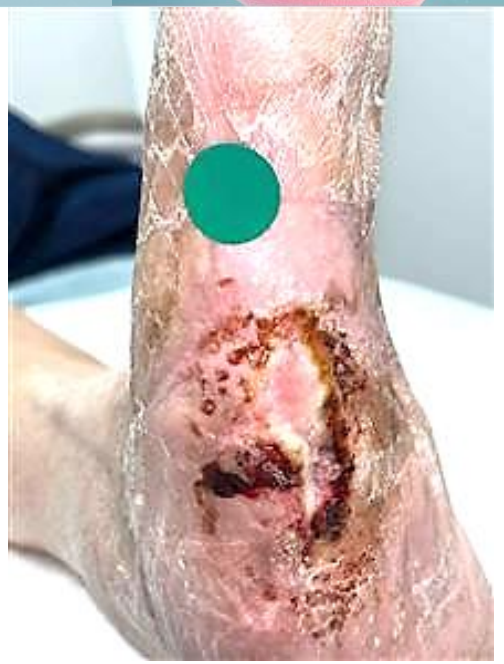
Patient #4-JB



08/23/24 #1

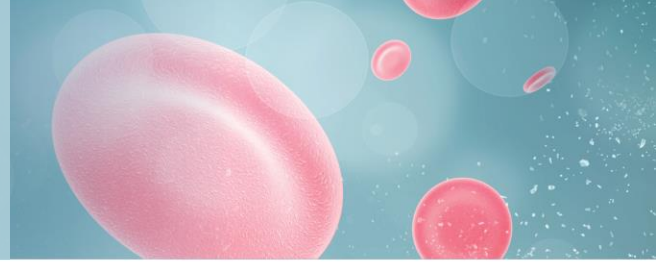


9/13/24
#4



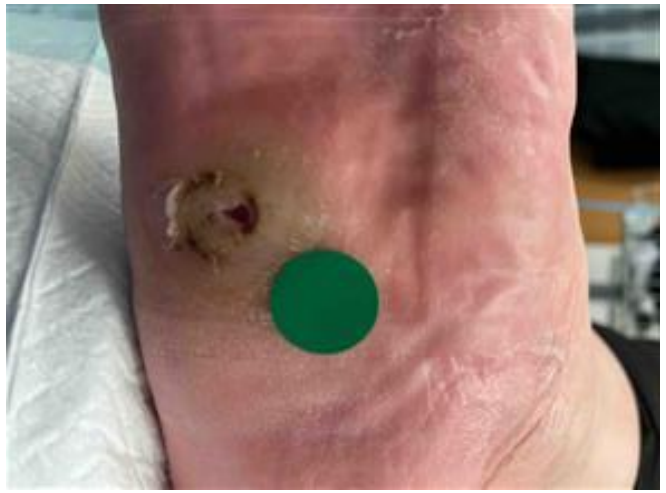
10/11/24 #8

Patient #5-AB

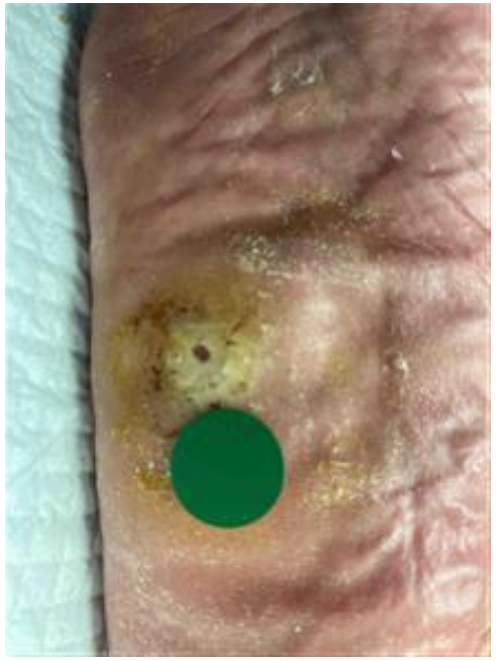


- 59 y/o Female
- PMH: DM II, HTN, CAD, Neuropathy
- Nonhealing ulceration.
- Noncompliant with offloading devices.
- After 4 weeks of conservative care ulceration remains unhealed.
- After 12 applications of the MLPF patch, site remains closed and stable with no reoccurrence
- Despite noncompliance with offloading during treatment

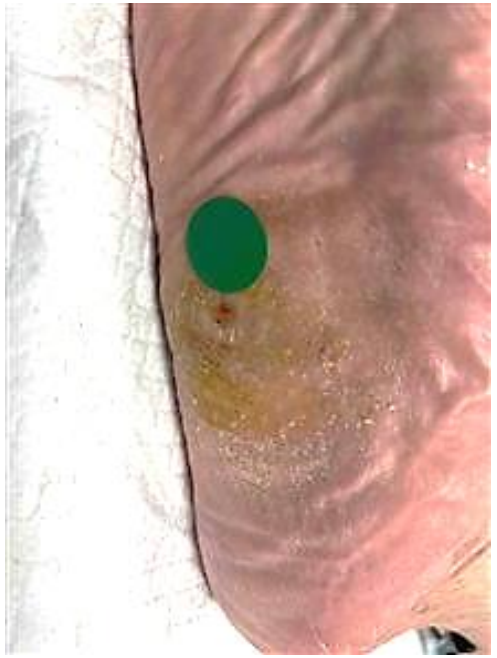
Patient #5-AB



12/13/24 #1



1/10/25 #5



3/14/25 #12

Patient Cases

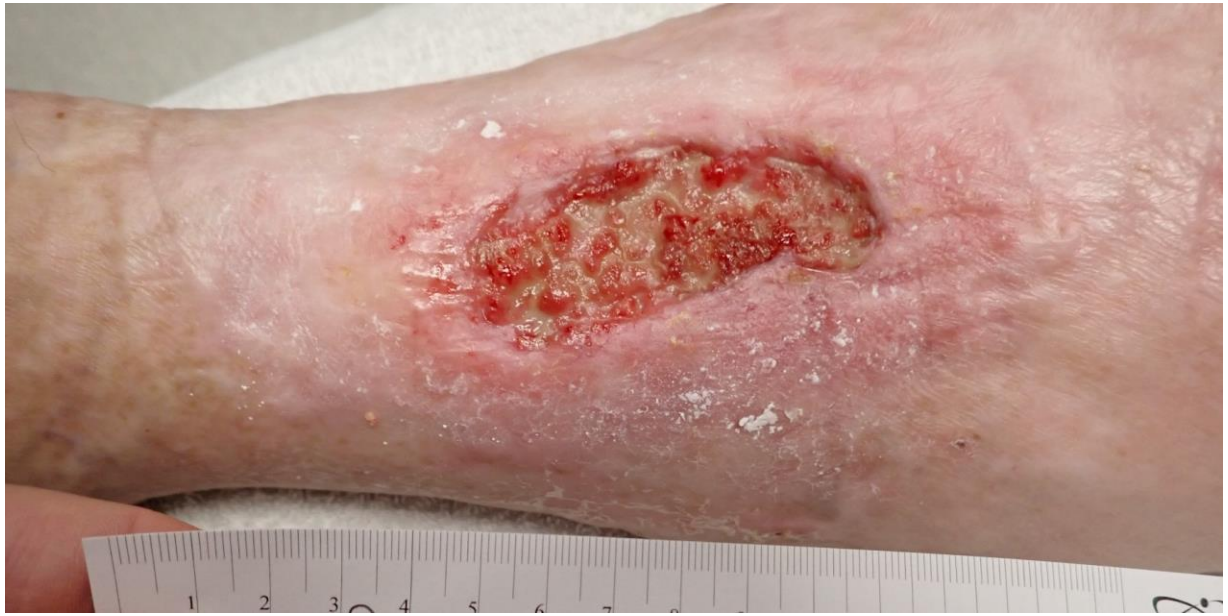
Tyson Green, DPM
James Y. Lin, DO

Mrs. Cookies

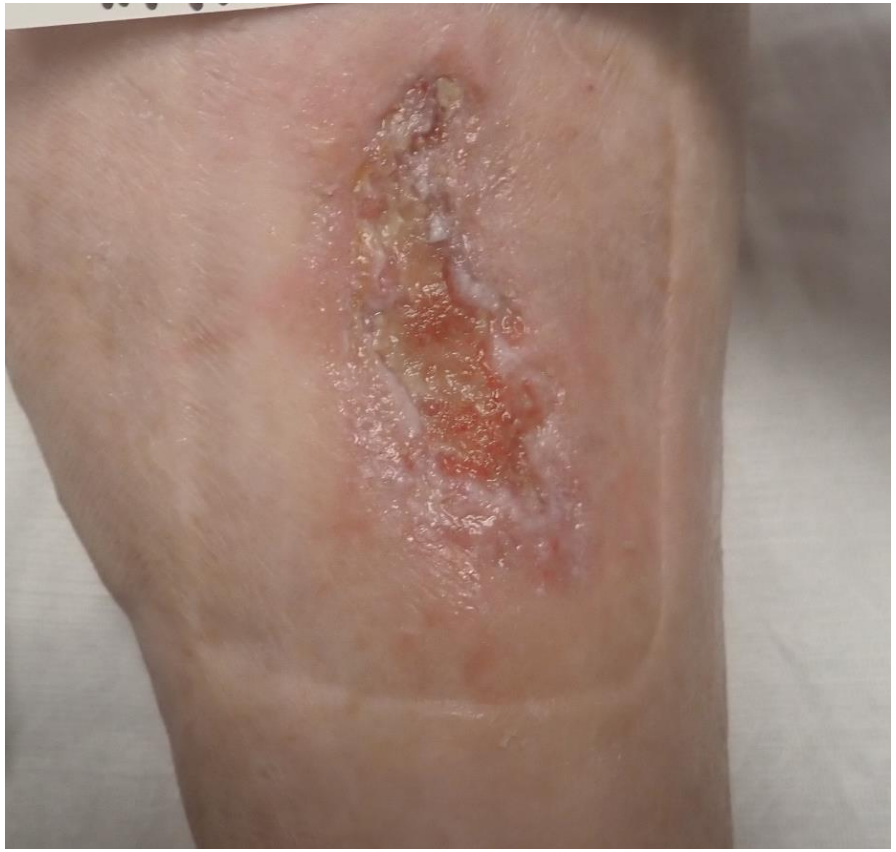
- 68 year old female
- Diabetes
- ESRD
- PVD
- Presented with wound to anterior tibia that has been present for 8 months after scraping it on an end table
- Seen weekly by home health for the last 3 months with Unna boot dressings applied

Mrs. Cookies

- Initial

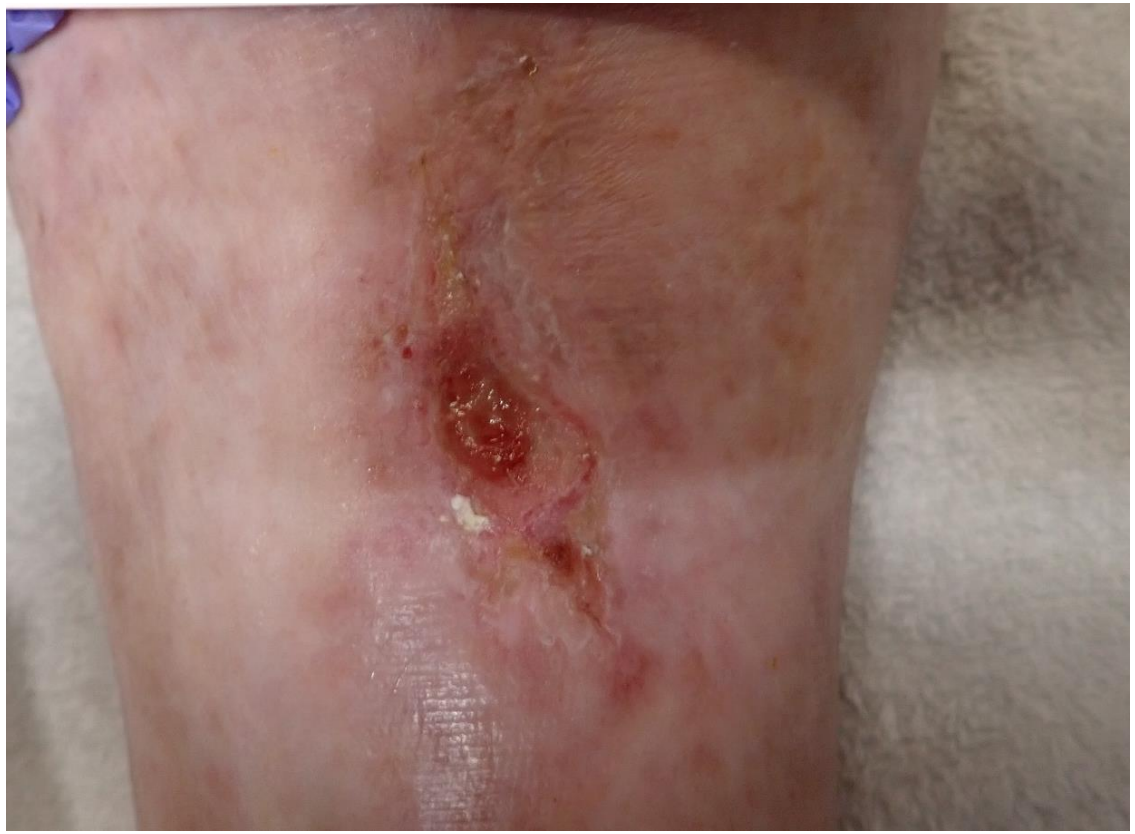


- 1 Week Follow-up - 1 Application

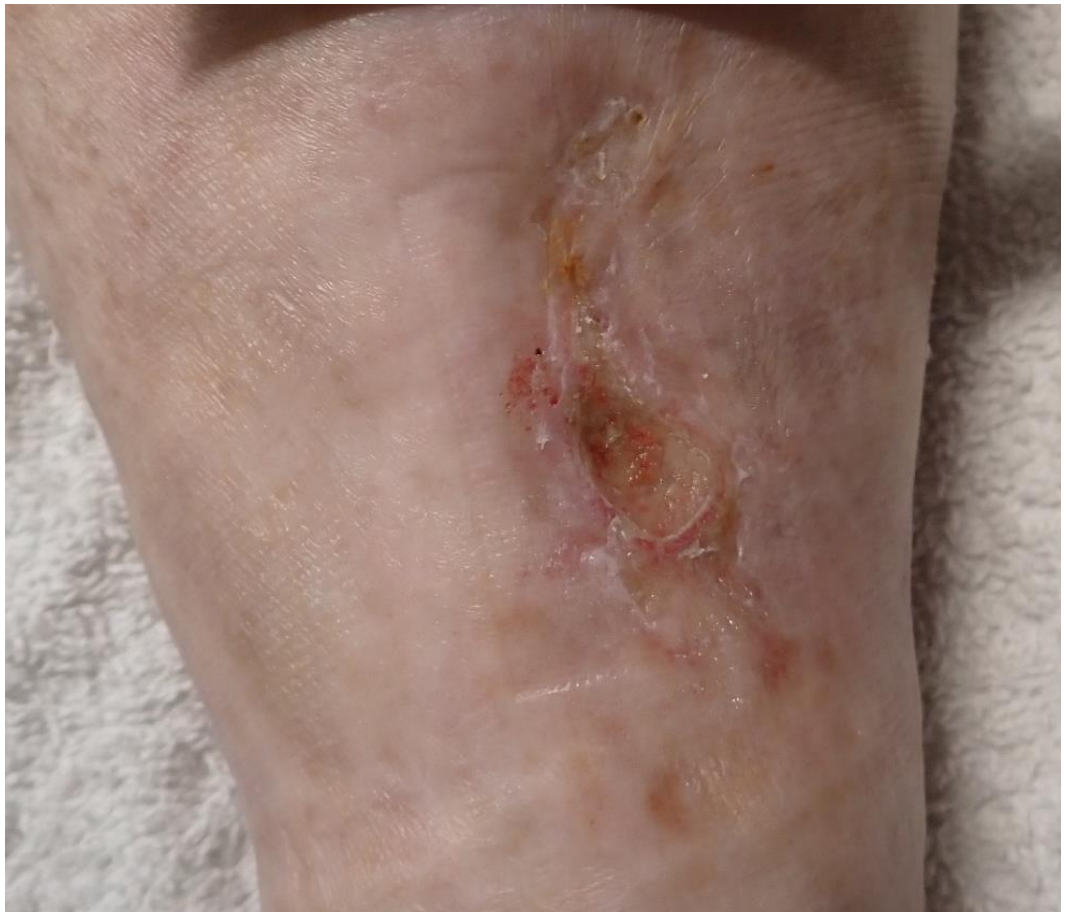


Mrs. Cookies

- Follow-up #2 – 2 applications



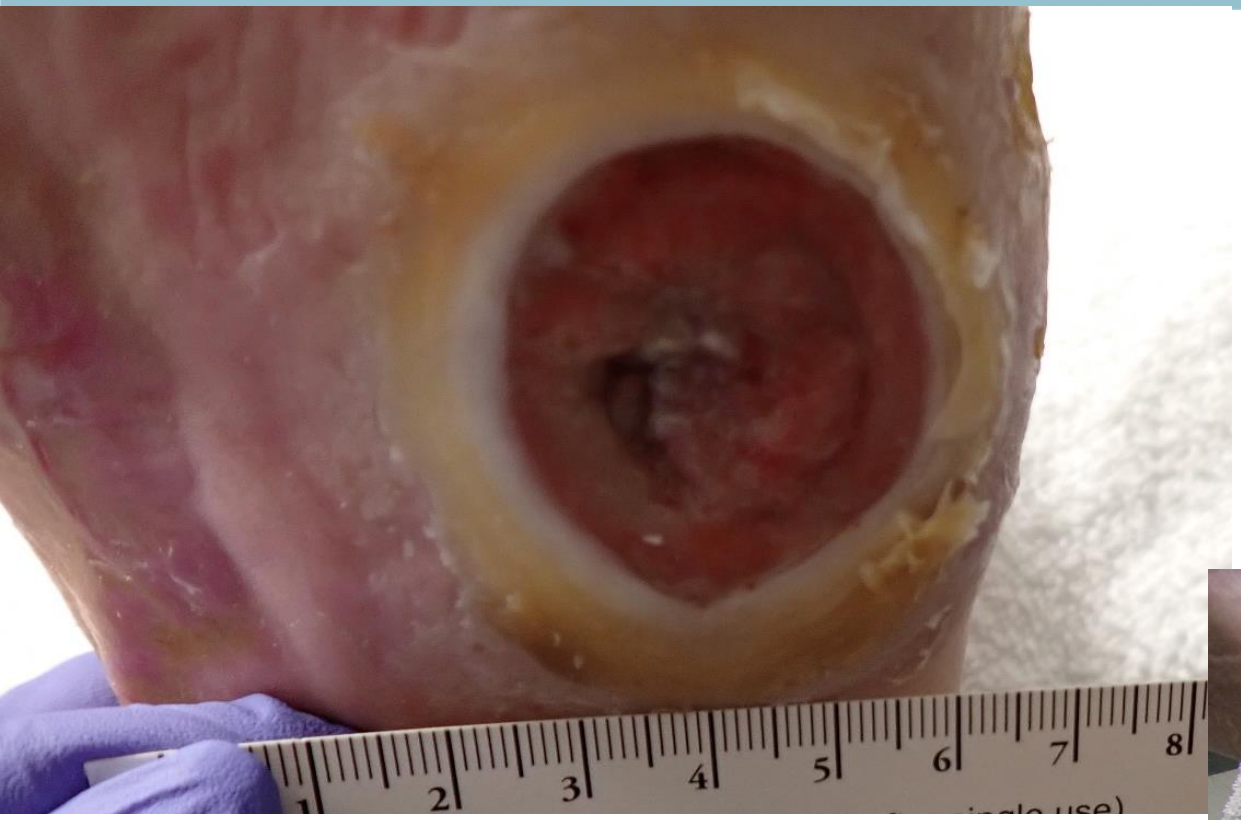
- Follow-up #3 – 3 applications



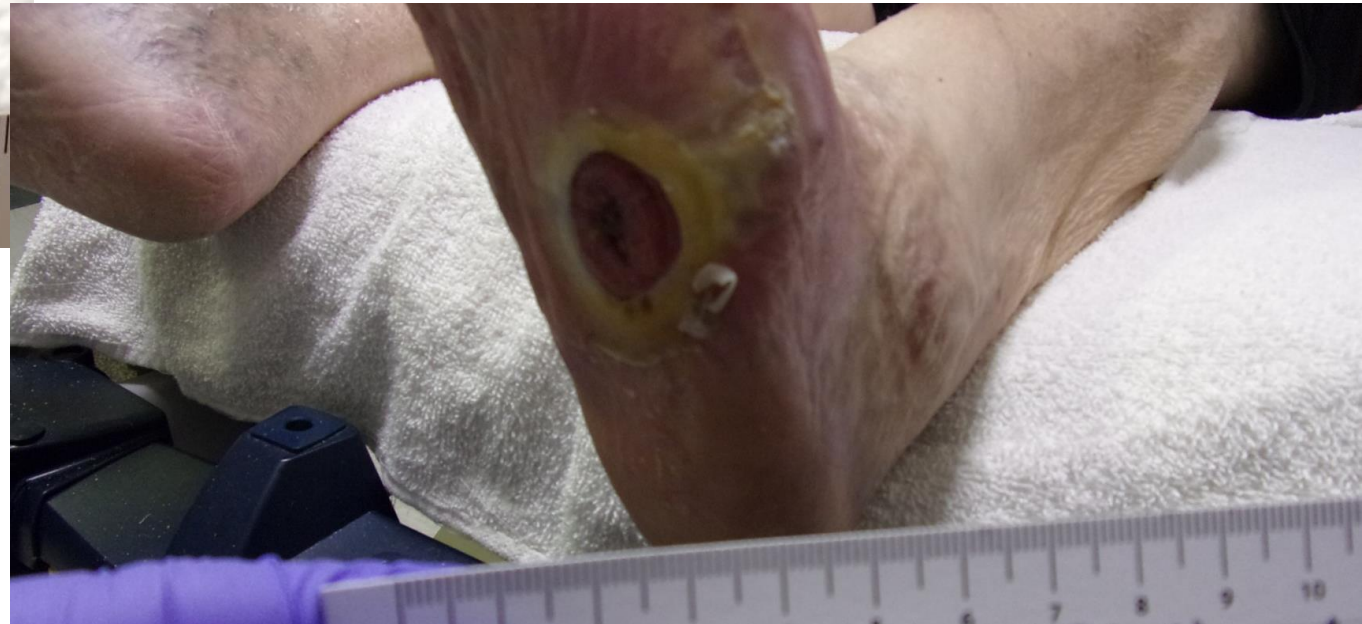
Mr. Flood

- 73 year old male
- Diabetes
- ESRD
- Charcot
- RA
- Presented with wound to plantar foot that has been present for “years”
- Made worse after the hurricane flooding it sat in water for over 12 hours

Mr. Flood

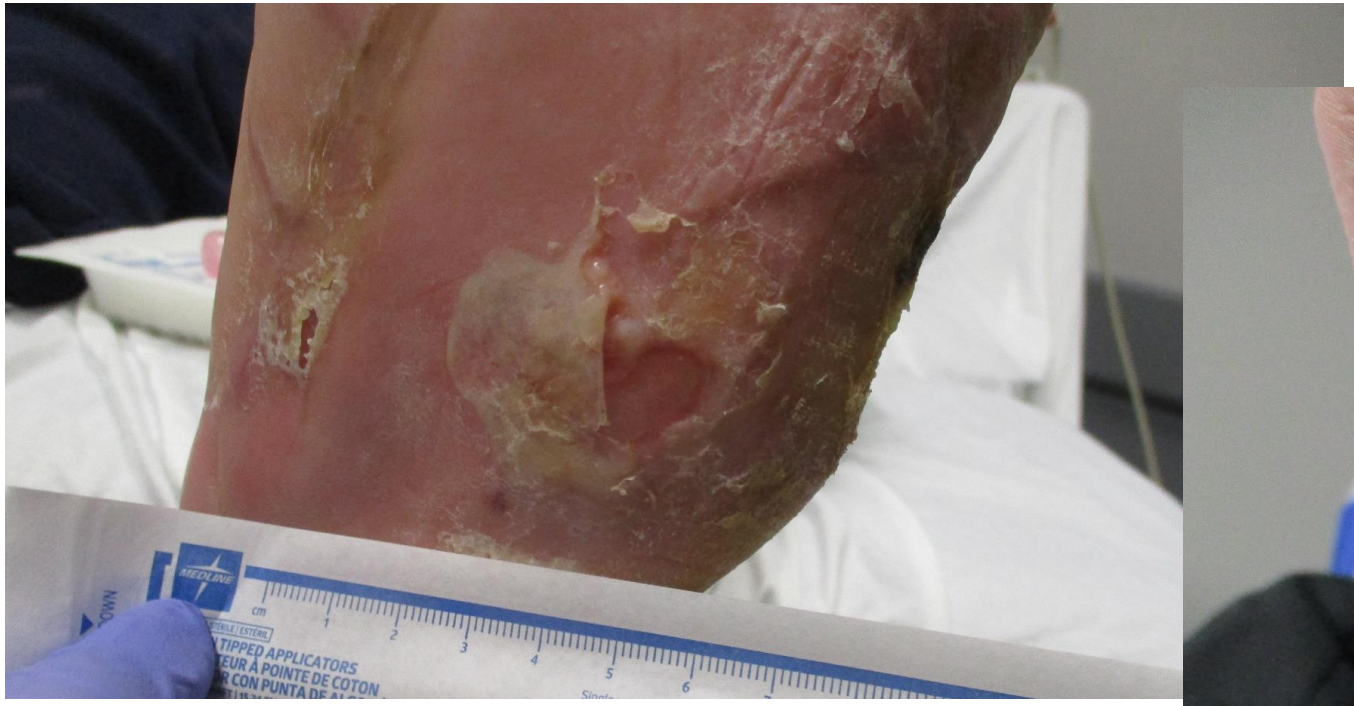


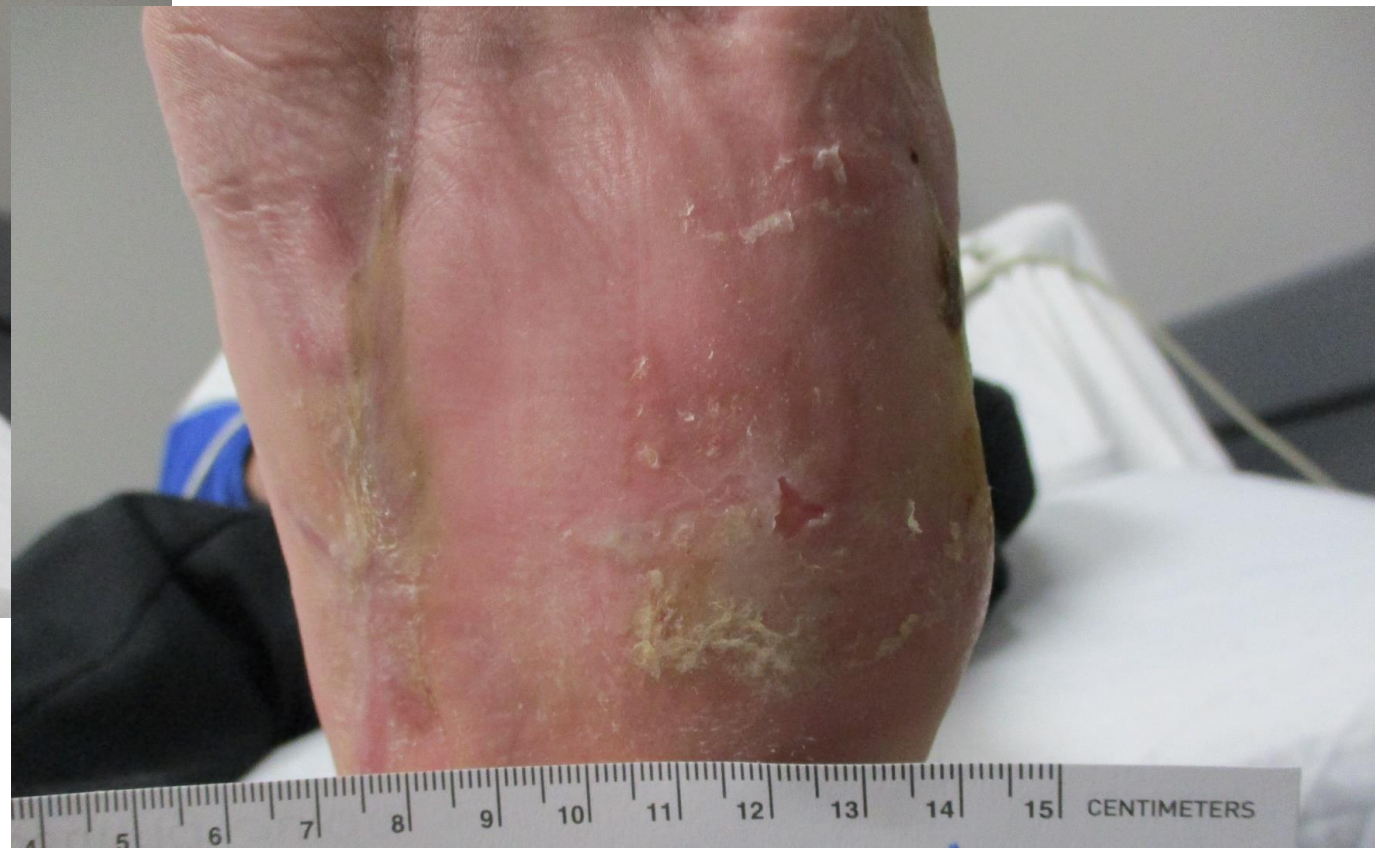
- Initial Visit



Mr. Flood

- 8 week follow-up – 3 applications





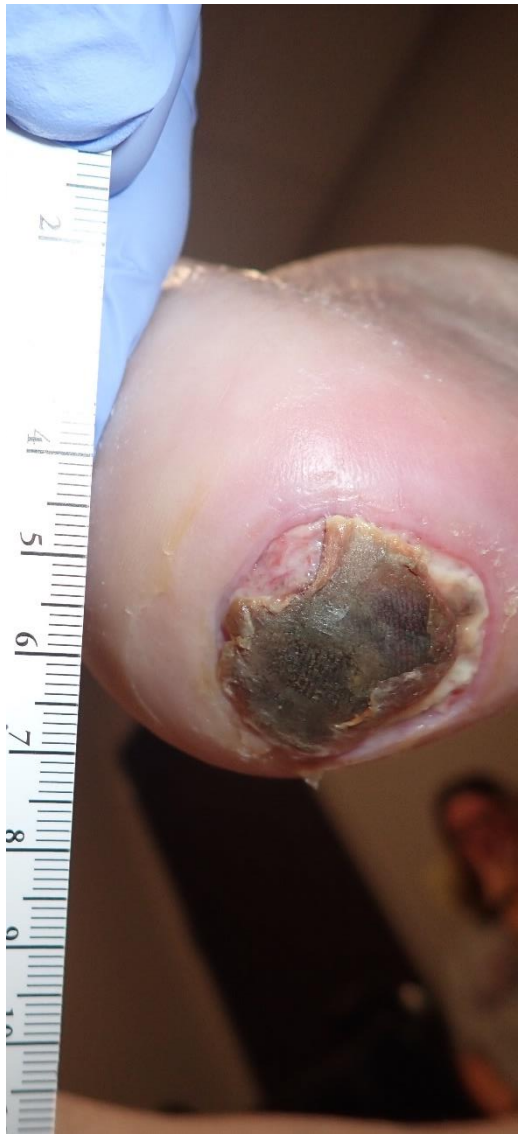
- 10 week follow-up – 4 applications

Mrs. Slippers

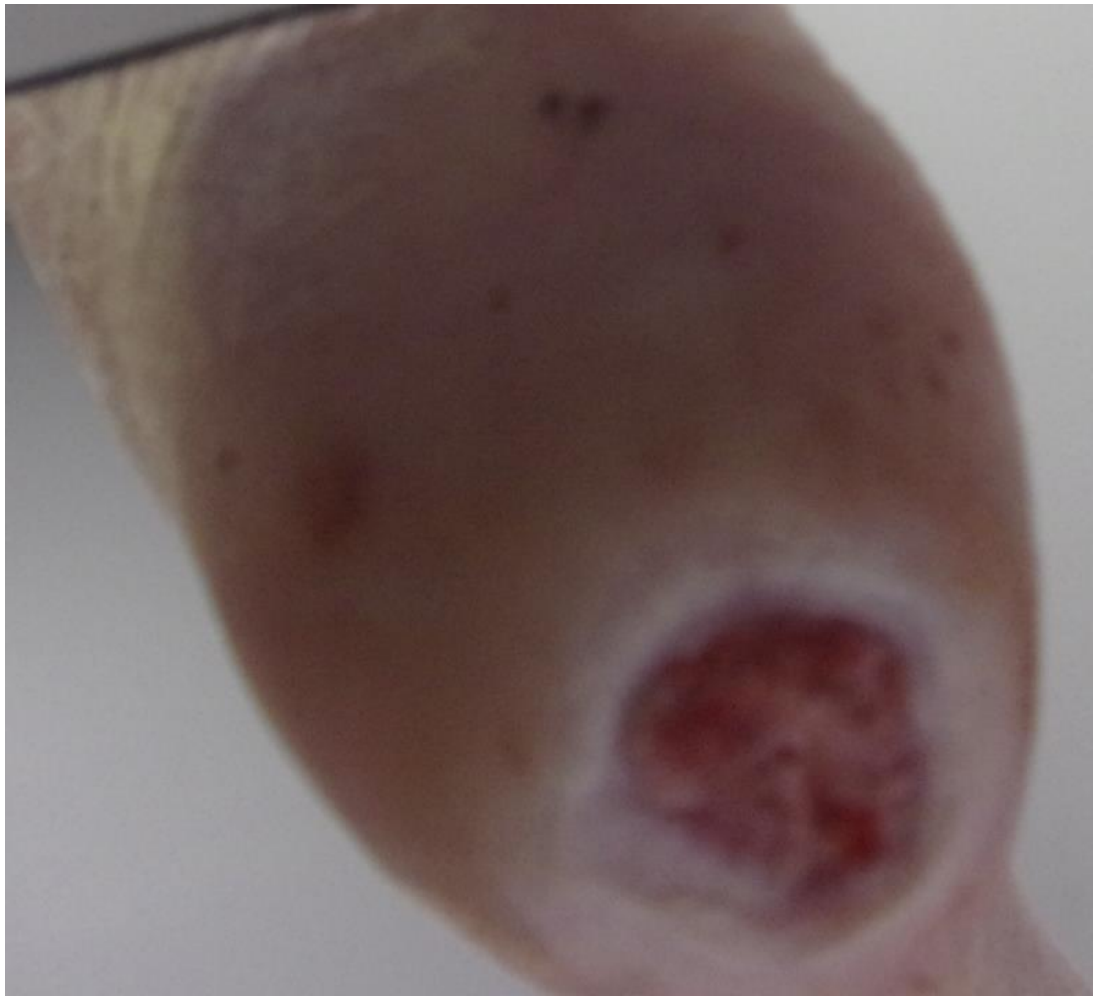
- 86 year old female
- Diabetes
- ESRD
- PVD
- Presented with wound to heel that she developed after she broke her hip
- Been the same size and severity for 18 months

Mrs. Slippers

- Initial

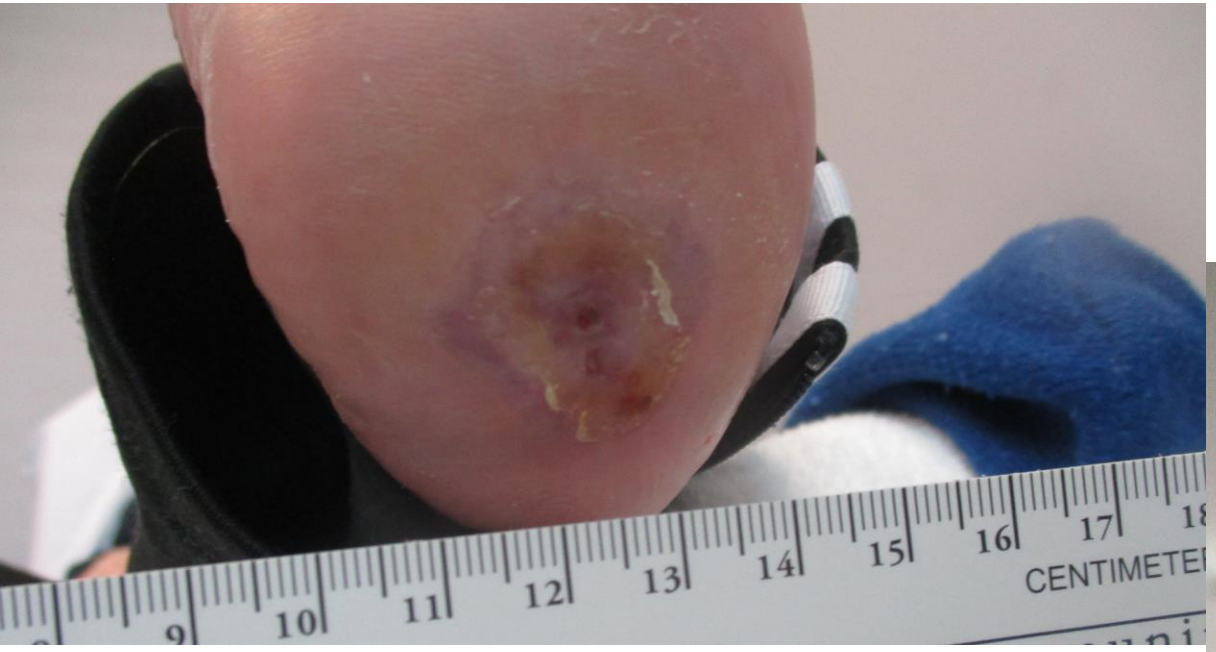


- 2 week follow-up – 1 application

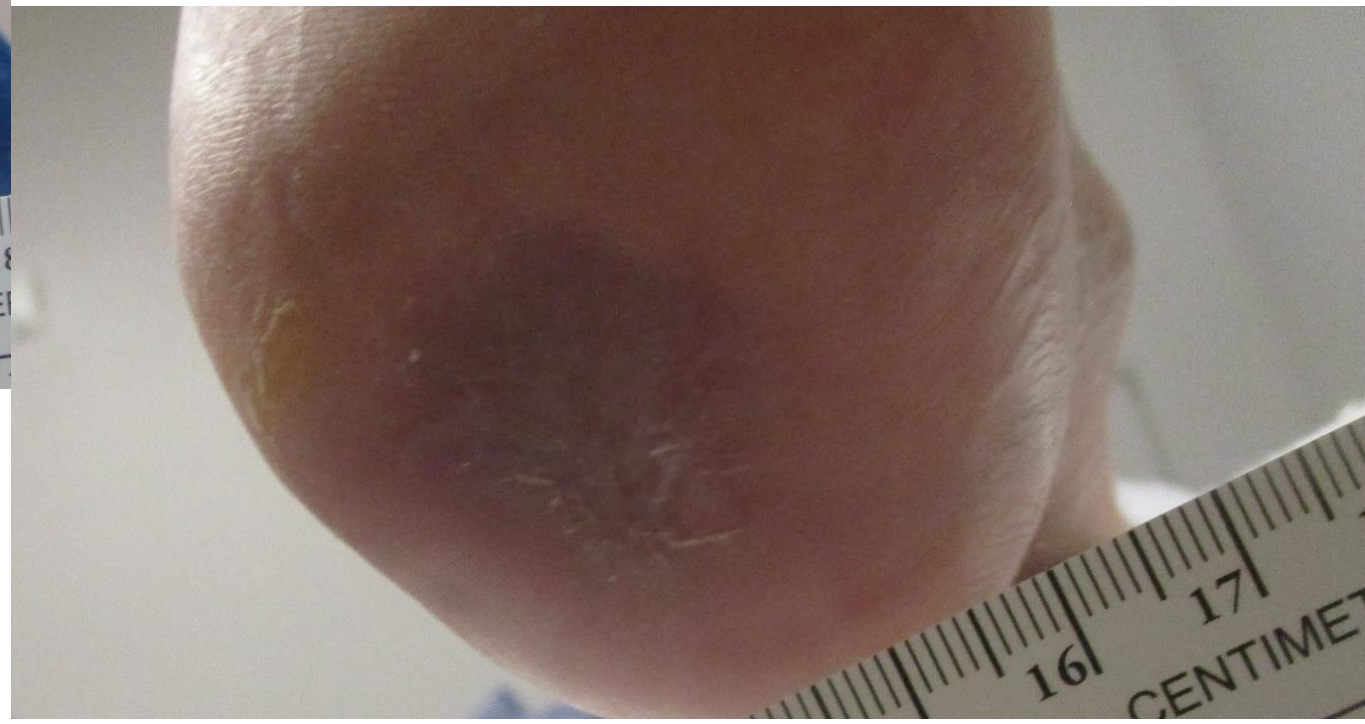


Mrs. Slippers

- 6 week follow-up – 3 applications



- 8 week follow-up – 4 applications



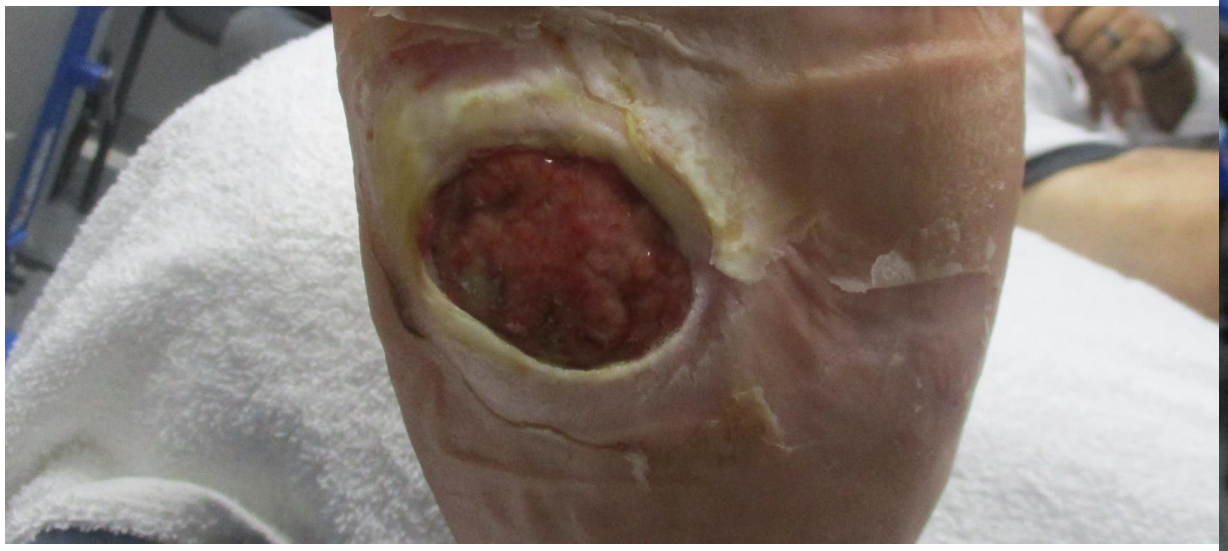
Mr. Hunter

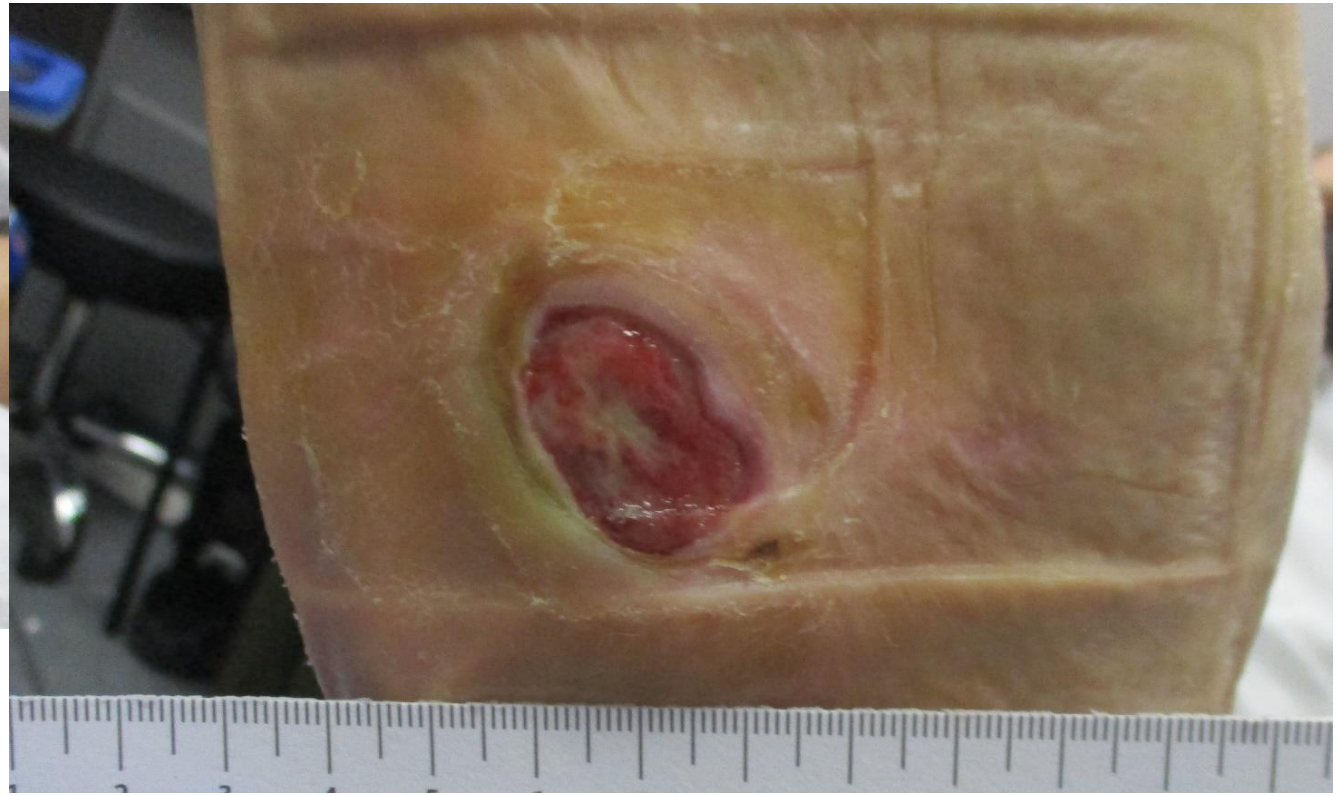
- 62 year old male
- Diabetes
- PVD
- Charcot
- Presented with wound to plantar foot that has been present for “years”
- Gets worse every duck hunting season

Mr. Hunter

- 2 week follow-up – 1 application!

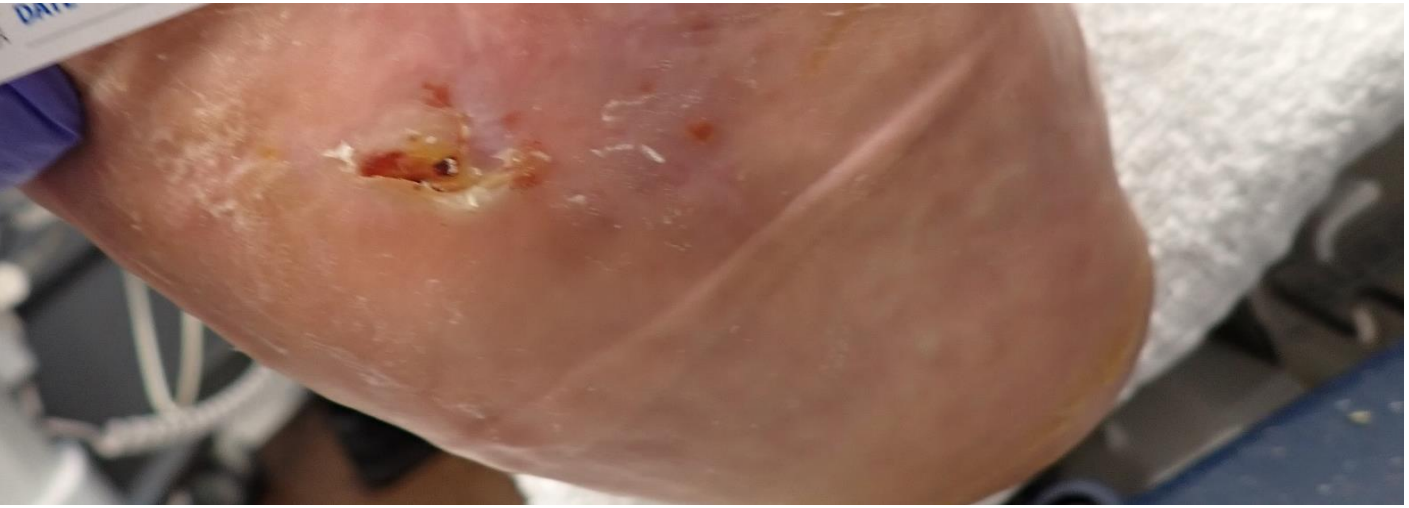
- Initial



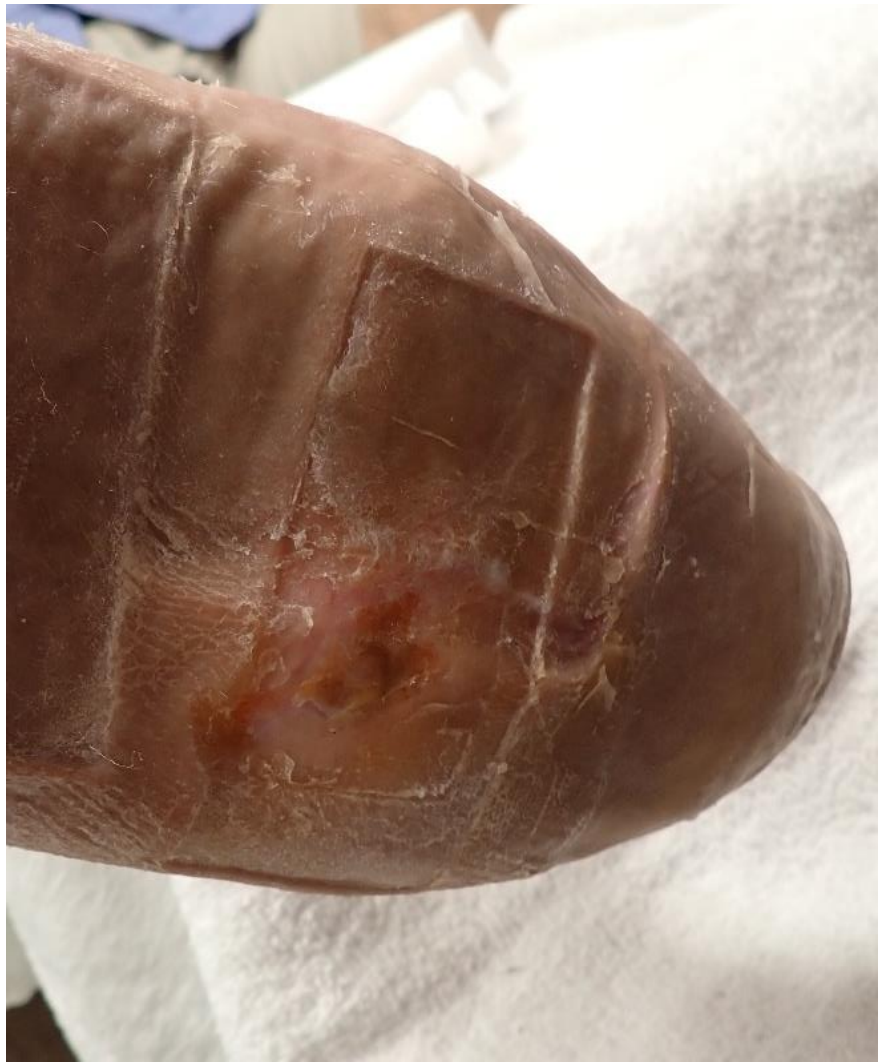


Mr. Hunter

- 6 week follow-up – 3 applications



- 10 week follow-up - 4 applications

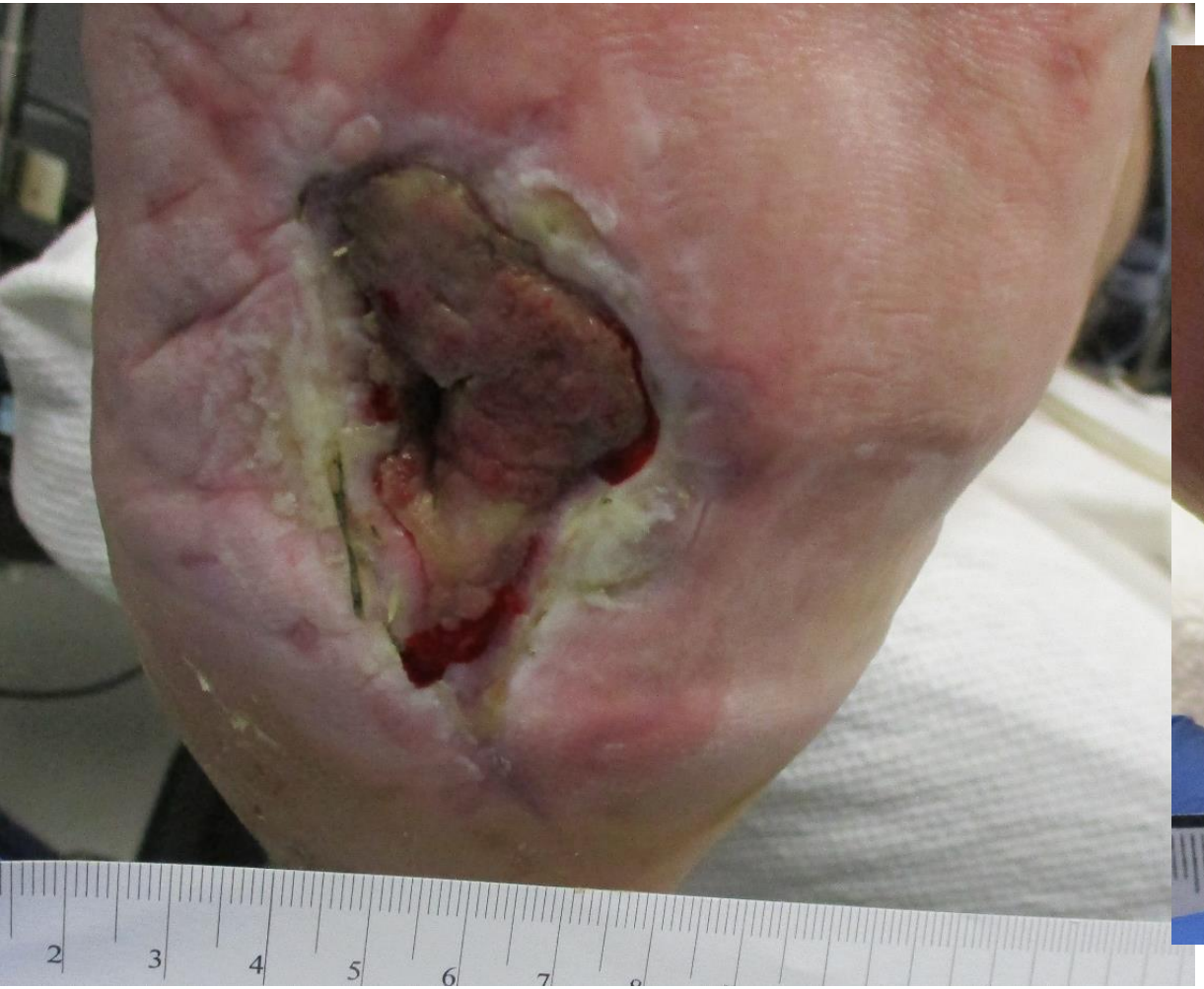


Mr. Joker

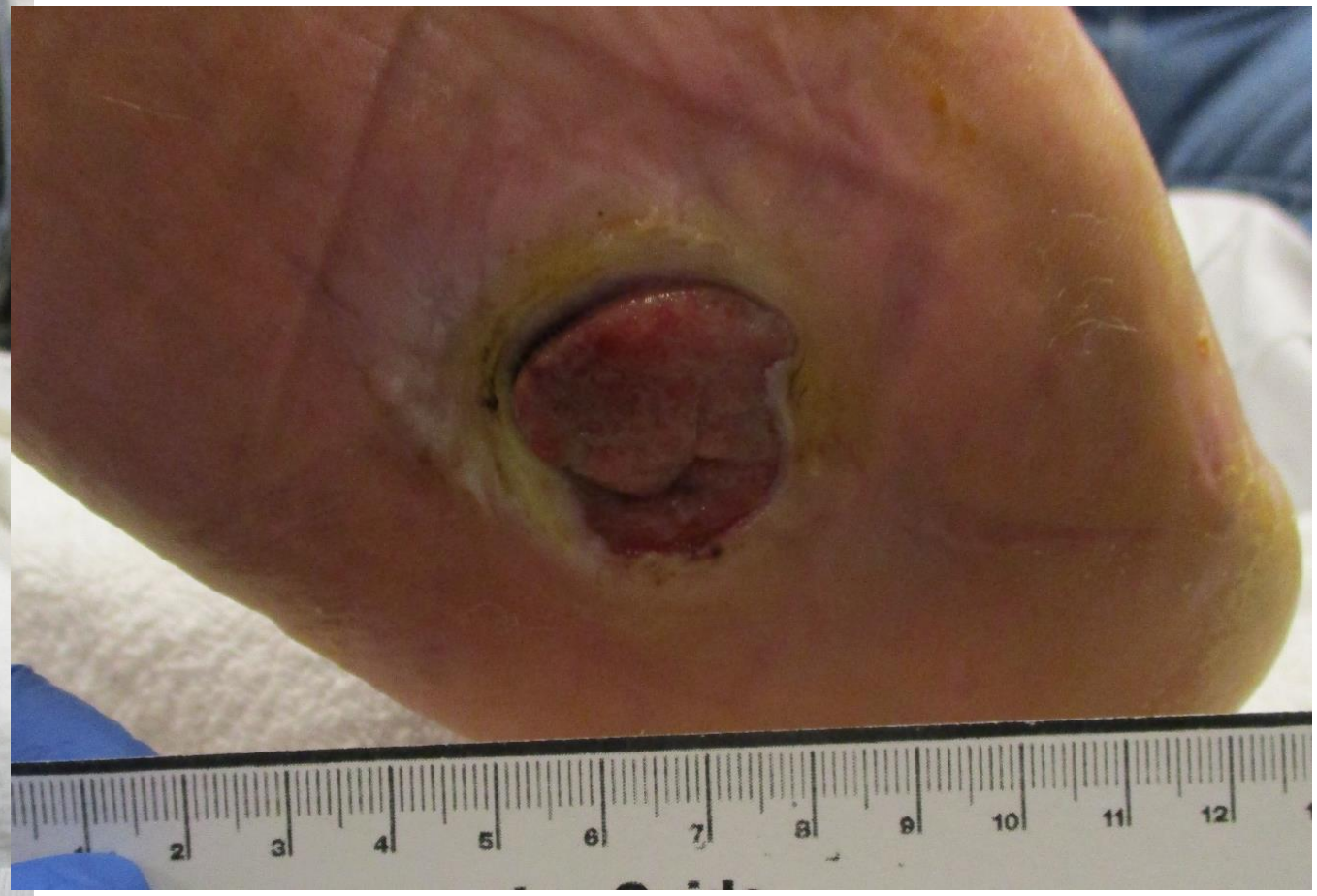
- 64 year old male
- Diabetes
- PVD
- Charcot
- Presented with wound to plantar foot that has been present for 6 years!
- Has “healed” several times but after recent osteomyelitis has gotten worse

Mr. Joker

- Initial

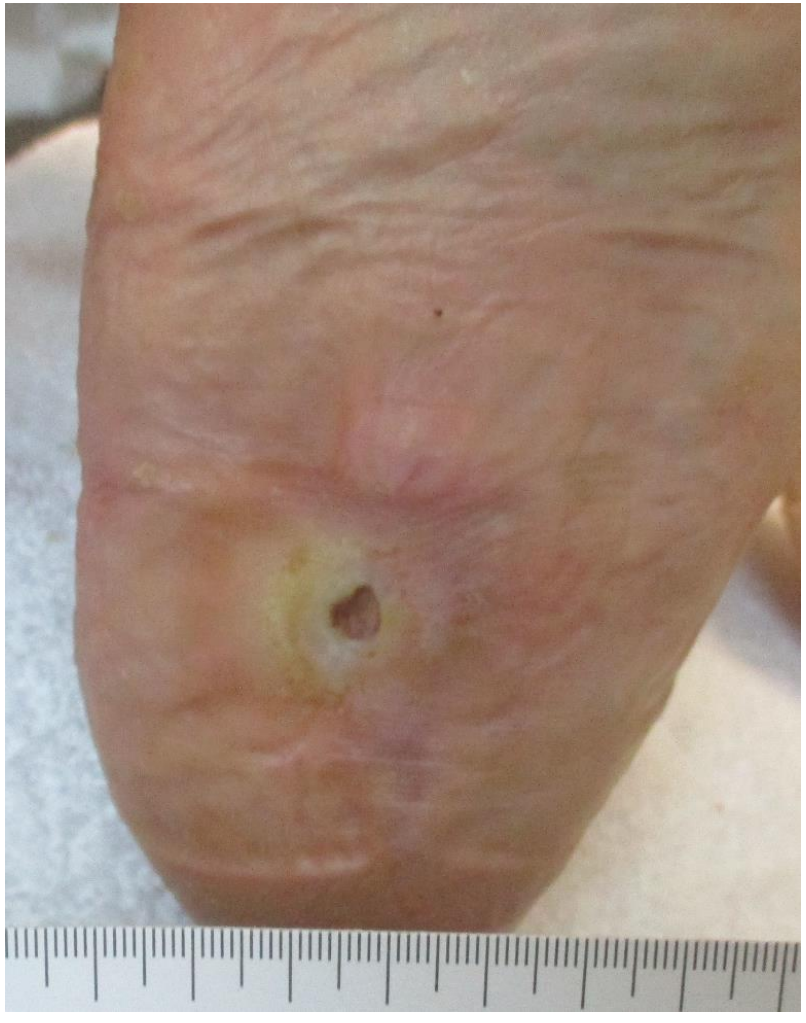


- 3 week follow-up – 2 applications

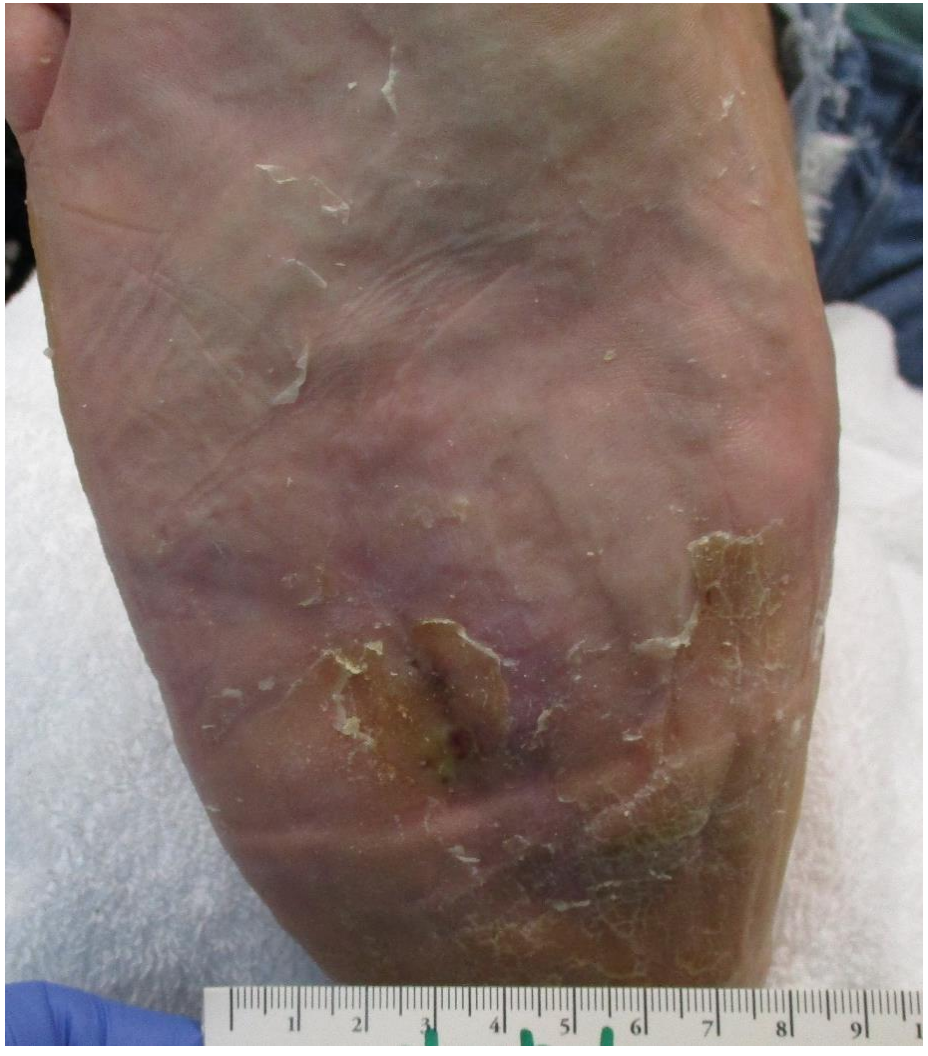


Mr. Joker

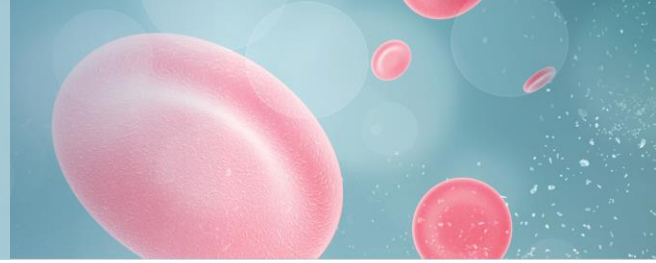
- 6 week follow-up – 4 applications



- 8 week follow-up – 6 applications



Patient response??



- “If I would have known that all it took was my own blood to heal it I would have done this a long time ago!” *-Mrs. Cookies*
- “I had no idea that my body had any healing properties in it anymore!” *–Mr. Flood*
- “I’m so happy to be healed but I still think I need several more follow-ups with my wound care husband!” – *Mrs. Slippers*
- *“*Thanks Doc…see you again after duck hunting season!” *–Mr. Hunter*
- “Can’t thank you enough for giving me more quality of life with my grandkids…or should I just be thanking myself?!” *–Mr. Joker*