ActiGraft PRO

Blood Derived Wound Care System

Table of Contents

ActiGraft^{PRO} Overview

A PERSONALIZED APPROACH TO **WOUND HEALING**

ActiGraft^{PRO} system is an innovative wound solution that uses a patient's own blood to create an autologous whole blood clot. Once applied, the blood clot serves as a protective covering and supports wound healing processes which naturally occur in the patient's body.

IS **ACTIGRAFT^{PRO}** THE RIGHT SOLUTION FOR YOUR FACILITY?

PROVEN OUTCOMES

173% more patients healed in the intervention arm compared to standard of care using Intent to treat (ITT) population, giving **odds ratio of 2.73.***

STREAMLINED PROCEDURE

Seamless process with **no centrifuge, 5-minute coagulation,** and the flexibility to draw and store blood up to 24 hours prior to the procedure.

NATURAL HEALING

Created from a patient's own peripheral whole blood, **even in the presence of blood thinners**, to provide the wound with an optimal, natural healing environment.

EASILY ADAPTABLE

Single application of the 28 cm^2 whole blood clot can be applied up to **56 cm^2** wound.

CHOOSE WITH CONFIDENCE

Described by NCD 270.3 as a blood derived product, ActiGraft^{PRO} is **eligible for Medicare and Medicare Advantage reimbursementt under G0465.** Commerical payor policies may vary.

AUTOLOGOUS

A personalized solution for patients with religious constraints, **immediately available at point of care.**

* www.magonlinelibrary.com/doi/full/10.12968/jowc.2024.0195

Challenges in Wound & Healthcare

LIFETIME RISK

25%

People with diabetes have a 25% lifetime risk of developing diabetic foot ulcers.[2]

CHRONIC

60%

Approximately 60% of all patients with diabetic foot ulcers develop wounds that become chronic.[3]

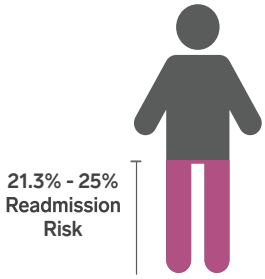
AMPUTATION

20%

For about 20% of patients, usual standard of care treatment ends with a devastating amputation within one year.[4]

INFECTION RATES

More than 10 million patients undergo surgical procedures as inpatients each year, accounting for over one-fourth of all hospital stays. Surgical site infection (SSI) occurs in 2-4% of all patients undergoing inpatient surgical procedures.[5]



READMISSION RATES

Lower extremity amputation has the highest readmission rate, surpassing 25% among Medicare patients greater than 65 years of age. Patients with diagnoses of “chronic ulceration” and “diabetes mellitus with complications” reportedly average readmission rates of 21.3 and 20.3%.[6]

COST & DISTRESS

Treating chronic wounds also has a substantial impact on the cost of care. If the severity of a wound progresses to grade 4 or 5, the cost of treatment is eight times higher than treating a grade 1 or 2 wound.[7] For most patients, the experience is debilitating. The longer the wound takes to heal, the greater the social isolation, and emotional and physical distress for the patient and their caregivers.[8]

1. Donner, B, et al. Analysis of Three Prospective, Open-Label, Clinical Trials with Autologous Blood Clot in Chronic Wounds. | 2. Boulton AJM, The Diabetic Foot, *Medicine* 43:1 2014 | 3. Stadler L, Wound Debridement – Robust Growth in a Dynamic Market, *SmartTRAK* 2018. | 4. Prompers L et al, Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and with-out peripheral arterial disease, *Diabetologia*, 2008; 51(5). | 5. P. (2019, September). Surgical site infections. Retrieved February, from https://psnet.ahrq.gov/primer/surgical-site-infections. | 6. King, K. (2018, August 28). A critical look at readmissions for patients with diabetic foot infections. Retrieved February 12, 2021. https://www.podiatrytoday.com/critical-look-readmissions-patients-diabetic-foot-infections | 7. Stevens P, The Cost of Diabetic Foot Ulcers, The O&P Edge, August 2015, seen 19 March 2019 in https://opedge.com/Articles/ViewArticle/2015-08_02. | 8. Järbrink K et al, The humanistic and economic burden of chronic wounds: a protocol for a systematic review, *Systematic Reviews* 6:15 2017. | 9. Snyder RJ, Schultz G, Wachuku C, Rashid AM, Ead JKK. Proposed Mechanism of Action of Topically Applied Autologous Blood Clot Tissue: A Quintessential Cellular and Tissue Based Therapy. *J Am Podiatr Med Assoc*. 2020 Oct 13:20-140. doi: 10.7547/20-140. Epub ahead of print. PMID: 33052392.4.0195

ActiGraft^{PRO} Clinical Trials

183% more patients healed in the intervention arm compared to standard of care using Per Protocol (PP) population, giving odds ratio of 2.83

ActiGraft

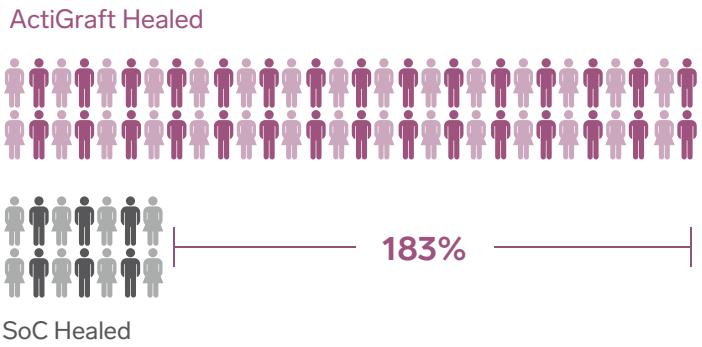
Arm Healed

2.83X

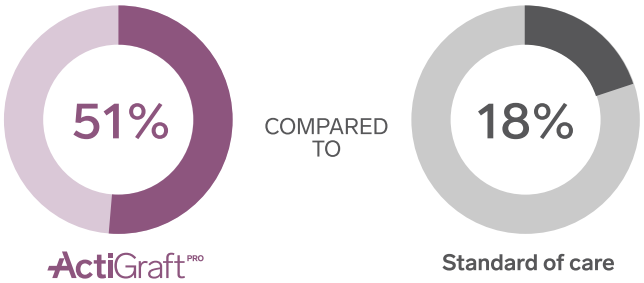
More than standard of care, with **faster and more duarable** healing outcomes

*per protocol (PP)

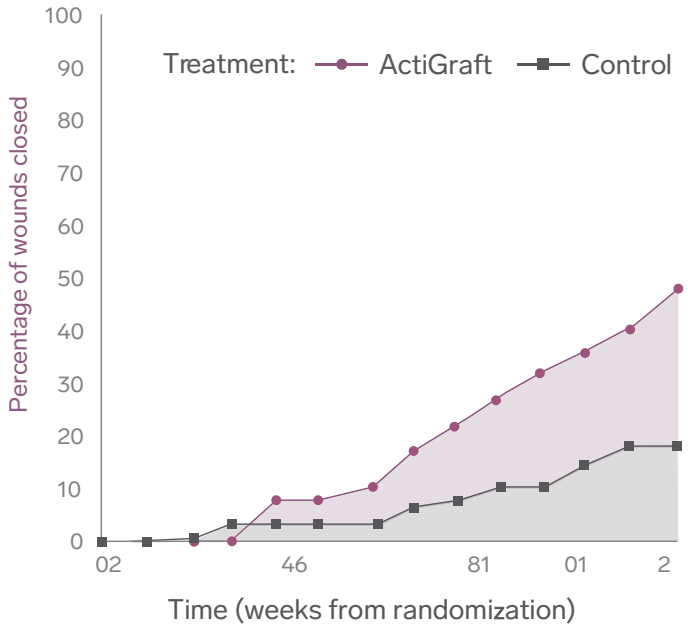
Complete Wound Closure (PP)



COMPLETE HEALING RATES BY 12 WEEKS
PER PROTOCOL (PP) POPULATION P=0.0075



Weekly Percentage of Wounds Closed (PP)



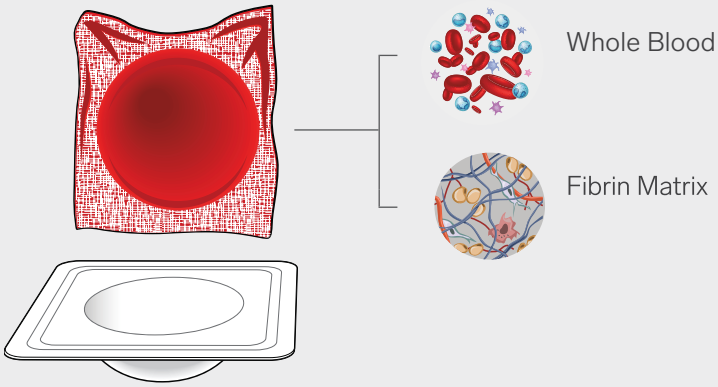
* www.magonlinelibrary.com/doi/full/10.12968/jowc.2024.0195

ActiGraft^{PRO} Mechanism of Action

RECREATING THE **NATURAL WOUND HEALING ENVIRONMENT**

ActiGraft^{PRO} Whole Blood Clot

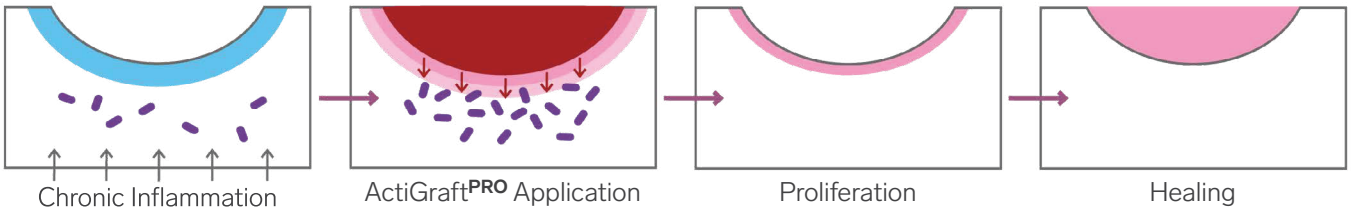
Derived from your patient's own blood, the ActiGraft^{PRO} Whole Blood Clot is embedded with essential wound healing elements, such as red blood cells, macrophages, platelets, proteins, clotting factors, minerals, electrolytes and dissolved gases, bound within a natural fibrin scaffold.



HOW **ACTIGRAFT^{PRO}** WORKS

ActiGraft^{PRO} is topically applied to your patient's wound site every 5-7 days. Once applied, it delivers biologically active elements to the wound bed and replaces the dysfunctional extracellular matrix - a leading culprit of stalled healing - with a provisional, functional fibrin matrix.

ActiGraft^{PRO} may reactivate the body's natural healing cascade that supports the wound healing process, accelerating your patient's road to recovery.



ACTIGRAFT^{PRO} INTENDED USE

The ActiGraft^{PRO} is intended to be used at point-of-care for the safe and rapid preparation of Whole Blood Clot (WBC) from a small sample of a patient's own peripheral blood. Under the supervision of a healthcare professional, the WBC produced by the ActiGraft^{PRO} is topically applied for the management of exuding cutaneous wounds, such as leg ulcers, pressure ulcers, diabetic ulcers, and mechanically or surgically-debrided wounds.

* https://japmaonline.org/view/journals/apms/113/3/20-140.xml

510(k) Letter

U.S. FOOD & DRUG ADMINISTRATION

June 22, 2021

RedDress Ltd
c/o Janice Hogan
Hogan Lovells US LLP
1735 Market Street, Suite 2300
Philadelphia, PA 19103

Re: BK210570
Trade/Device Name: RD2 Ver.02 System
Regulation Number: 21 CFR 864.9245
Regulation Name: Automated blood cell separator
Regulatory Class: Class II
Common Name: Peripheral Blood Processing Device For Wound Management
Product Code: PMQ
Dated: March 24, 2021
Received: March 24, 2021

Dear Ms. Hogan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801) medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Wilson Bryan -S

Digitally signed by Wilson Bryan -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Wilson Bryan -S, 0.9.2342.19200300.100.1.1=2001265579
Date: 2021.06.22 13:20:10 -04'00'

Wilson W. Bryan, MD
Director
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

Enclosure

Indications for Use (CBER/OTAT)

510(k) Number: BK210570

Device Name: RD2 Ver.02 System

Indications for Use: The RD2 Ver.02 System is intended to be used at point-of-care for the safe and rapid preparation of Whole Blood Clot (WBC) from a small sample of a patient's own peripheral blood. Under the supervision of a healthcare professional, the WBC produced by the RD2 Ver.02 System is topically applied for the management of exuding cutaneous wounds, such as leg ulcers, pressure ulcers, diabetic ulcers, and mechanically or surgically-debrided wounds.

Prescription Use _X_ (Part 21 CFR 801 Subpart D) AND/OR **Over-The-Counter Use** ____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE- CONTINUE ANOTHER PAGE IF NEEDED)

Concurrence of CBER, Office of Tissues and Advanced Therapies

Wilson Bryan -S

Digitally signed by Wilson Bryan -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Wilson Bryan -S, 0.9.2342.19200300.100.1.1=2001265579
Date: 2021.06.22 13:18:46 -04'00'

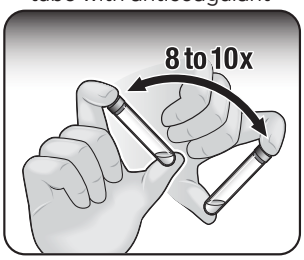
Office Sign-Off
Office of Tissues and Advanced Therapies

510(k): BK 210570

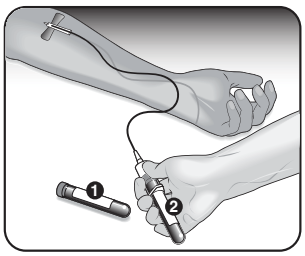
ActiGraft^{PRO} Instructions For Use

QUICK, **SIMPLE** AND **SEAMLESSLY INTEGRATION** INTO CURRENT TREATMENT PRACTICES

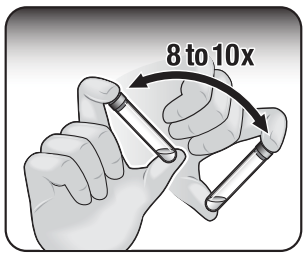
1. Agitate the tube to coat tube with anticoagulant



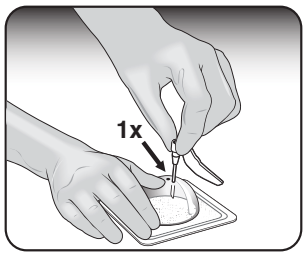
2. Draw blood



3. Gently shake immediately after blood draw to mix well

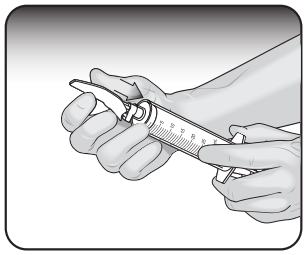


4. Pierce blister once for air outlet

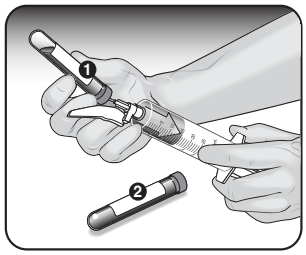


5. Dispose of needle

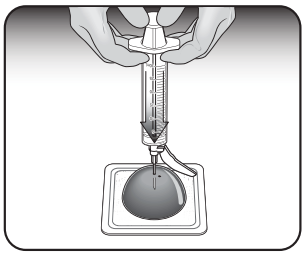
6. Attach 2nd safety needle



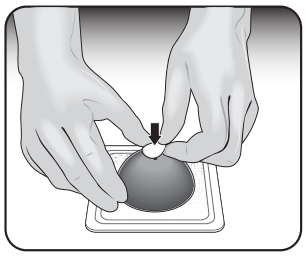
7. Draw 20ml of blood to safety needle



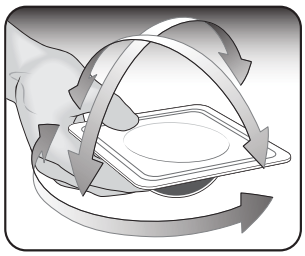
8. Inject blood through blister hole



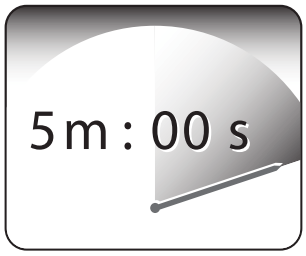
9. Clean and seal hubs



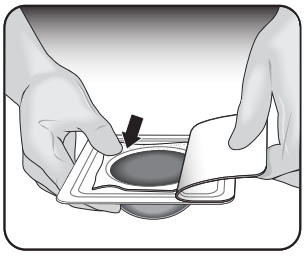
10. Mix contents



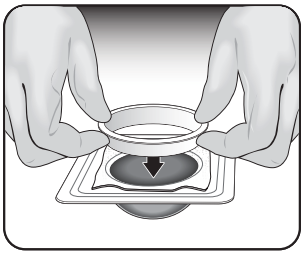
11. Allow at least 5 minutes for coagulation



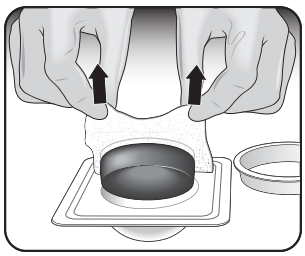
12. Secure gauze while removing backing



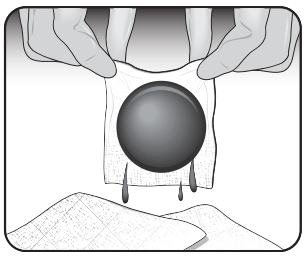
13. Loosen clot with ring



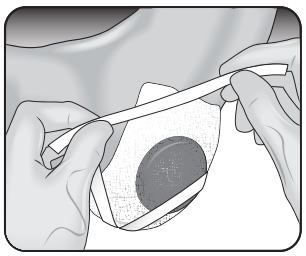
14. Lift clot holding gauze corners



15. Drain excess solution



16. Apply clot directly to wound



17. Complete all required documentation

REF: LBL-QG-0003 Rev.2

For safety information, visit www.legacymedicalconsultants.com/actigraft-safety-info

To view the ActiGraft^{PRO} Procedure Video, visit: **reddressmedical.com/actigraftpro**

ActiGraft^{PRO} Reimbursement

ActiGraft^{PRO} is now eligible for reimbursement nationally from Medicare and Medicare Advantage. ActiGraft^{PRO} is described by NCD 270.3 as a blood-derived product for chronic, non-healing wounds and is eligible for reimbursement under the G0465 procedure code. **ActiGraft^{PRO} is NOT a skin substitute/CTP.**

Under G0465, diabetic patients, non-pressure chronic injuries on Medicare are eligible for ActiGraft^{PRO} reimbursement. Key highlights of ActiGraft^{PRO}'s reimbursement status include:

- Up to 20 weeks of coverage
- G0465 has no exclusion for exposed bone and tendon
- Multiple procedure rules apply
- If applicable, providers may bill G0465 for application outpatient wound centers

Hospital Outpatient Reimbursement – OPPS Schedule

HCPCS Code	HCPCS Description	Status Indicator	APC	Medicare National Average Payment
G0465	Autologous platelet rich plasma (PRP) or other blood-derived product for diabetic chronic wounds/ulcers, using an FDA-cleared device for this indication, (Includes as applicable administration, dressings, phlebotomy, centrifugation or mixing, and all other preparatory procedures, per treatment)	T	5054	$2,107.97

Provider In-Facility Reimbursement – MPFS Schedule

HCPCS Code	HCPCS Description	MPFS Status Code	Medicare National Payment (Facility)
G0465	Autologous platelet rich plasma (PRP) or other blood-derived product for diabetic chronic wounds/ulcers, using an FDA-cleared device for this indication, (Includes as applicable administration, dressings, phlebotomy, centrifugation or mixing, and all other preparatory procedures, per treatment)	A	$83.84

Starting in 2025, Physician payment rates have been established by CMS for HCPCS code G0465. Please note that CMS wage Index may affect MPFS published rates.

Testimonials

WHAT OUR CLIENTS ARE SAYING

"We conducted a clinical evaluation on two different male patients with diabetic foot ulcers that have been recurrent for 2 or more years. After 4 weekly treatments, ActiGraft had facilitated the resolution of both wounds. ActiGraft has proven to be an efficient and both, time and a cost-effective solution to chronic, stalled and vascularly compromised wounds.

– **Georgeanne Botek, DPM**
Cleveland Clinic

"ActiGraft autologous blood tissue provides a unique wound care therapy that is both effective and cost efficient. As an adjunct to wound bed preparation, ActiGraft represents an important modality in expediting wound closure in many of my patients in both randomized controlled trials and clinical practice. I would highly recommend ActiGraft to other clinicians. This lower cost, fast healing solution has the potential to change the standard of care and the associated cost structures/budgets."

– **Robert J. Snyder, DPM**
Barry University of Podiatric Medicine

"I endorse ActiGraft as it uses the body's own healing cascade to help initiate the wound healing process, and has a unique role as a topical dressing in the wound care space."

– **Dr. Bryan Doner, DO**
D&P Medical Group

"ActiGraft provides a very unique wound care solution. ActiGraft was able to heal our surgical wounds, all while making the patient happier and more compliant in their after-surgery-care.

ActiGraft is truly a win-win solution for patients, practitioners and hospitals. I would highly recommend ActiGraft to other clinicians and to government entities"

– **Adil Kabeer, M.D.**
The Orthopedic Institute

"I was impressed with the the consistent improvement in wound healing week to week with ActiGraft. I will be looking for more patients to switch to ActiGraft in my practice because beyond the results, the support I got from the company went above and beyond."

– **Dr. Claire S., M.D.**
Melrose Surgical Associates

"In my experience ActiGraft delivered fantasic results for my patients. We were able to truly heal some of the most difficult wounds in a short amount of time. It gave us great satisfaction to be able to heal these very chronic non-healing wounds.

– **Dr. Naz Wahab, M.D.**
Wound Care Experts

"I recommend this to anybody that had a sore like I had for so long."

– **Ellen S., Patient**
West Revere Health Center

Peer-Reviewed Articles

ActiGraft

Real-world outcomes of autologous whole blood clot therapy for venous leg ulcers[20]

Author(s): Stephen Heisler, DPM, Assistant Professor; Rodney Samaan, MD, Cardiologist; Rene Lessing, RN, Wound Care Specialist; Emre Ozker, MD, Associate Professor; Robert Snyder, DPM, Professor and Director of Clinical Research

Link: https://www.magonlinelibrary.com/doi/abs/10.12968/jowc.2025.0419

Summary:

Venous leg ulcers (VLUs) are hard-to-heal wounds primarily caused by venous insufficiency and venous hypertension. These wounds pose significant clinical and economic burdens, often failing to heal with standard compression therapy alone. Autologous whole blood clot (AWBC) therapy has emerged as a potential treatment for hard-to-heal wounds, complementing the body's natural wound healing mechanisms. This study aims to evaluate the outcomes of AWBC in a real-world setting for treating VLUs that have not responded to conventional therapies.

A Multicenter, Prospective, Randomized, Controlled, Trial, Comparing the Safety and Efficacy of Autologous Whole Blood Clot to Standard of Care in Patients with Chronic Diabetic Foot Ulcers[19]

Author(s): Robert Snyder, Aksone Nouvong, Jesus Ulloa, Naz Wahab, Terry Treadwell, Febe Bruwer, Liezl Naude, James McGuire, Alexander M Reyzelman, Timothy Graham, Rene Lessing, Eric Lullove, Emre Ozker, Hau T Pham, Michael Pasternac, Shira Cohen

Link: https://doi.org/10.12968/jowc.2024.0195

Summary:

Diabetic foot ulcers (DFUs) present a significant global health challenge, resulting in high morbidity and economic costs. Current treatments often fail to achieve satisfactory healing rates, highlighting the need for novel therapies. This study evaluates the safety and efficacy of a novel autologous whole blood clot (AWBC), a blood-based, biodegradable provisional matrix in conjunction with standard care compared to standard care alone in treating chronic DFUs. This RCT demonstrated the safety and efficacy of AWBC in achieving wound closure compared to the best practice standard of care in hard-to-heal DFUs. AWBC had statistically significant healing outcomes compared to control, presenting a promising and innovative treatment for hard-to-heal DFUs, thus offering a significant improvement over traditional care. This novel approach addresses the underlying challenges in the wound microenvironment, suggesting a paradigm shift in managing chronic DFUs, and emphasizing the advantages and benefits of this innovative treatment.

Efficacy And Safety Of RD2 Ver.02, A Whole Blood Clot Therapy, Coupled With A Minimally Invasive Procedure In Pilonidal Sinus: A Phase II Study[18]

Author(s): Edward Ram, Yaniv Zager, Dan Carter, Roi Anteby, Josef Haik, Ido Nachmany, Nir Horesh

Link: https://doi.org/10.1007/s10151-024-02973-9

Summary:

Background PNS is caused by an infection in the sacrococcygeal area triggered by hair particle accumulation in skin tunnels, resulting in infection. Surgical options range from simple excision to complex flap constructions. Primary wound healing failure and recurrence rates contribute to the burden of PNS. RD2 Ver.02, a novel autologous whole-blood clot product, demonstrated safety and efficacy in treating complex cutaneous wounds and was investigated for the management of PNS.

Nerve Reconstruction Using ActiGraft BloodClot in Rabbit Acute Peripheral Injury Model: Preliminary Study. Bioengineering 2024, 11, 298[17]

Author(s): Simon Rochkind, Sharon Sirota, Alon Kushnir

Link: https://doi.org/10.3390/bioengineering11040298

Summary:

This preliminary study aimed to investigate an ActiGraft blood clot implant (RedDress Ltd., Pardes-Hanna, Israel) attempting to treat and induce the regeneration of a completely injured peripheral nerve with a massive loss defect. The results of this preliminary study suggest that applying an ActiGraft blood clot (into the collagen tube) can enable nerve recovery. This rigorous scientific inquiry contributes to additional valuable insights into the ongoing pursuit of innovative solutions for enhancing nerve regeneration and recovery.

A Prospective, Single-Arm Study To Evaluate The Safety And Efficacy Of RD2-VER.02, An Autologous Blood Clot, In The Treatment Of Anal Fistula[16]

Author(s): Edward Ram, Yaniv Zager, Dan Carter, Olga Saukhat, Roi Anteby, Ido Nachmany, Nir Horeshtt

Link: https://journals.lww.com/dcrjournal/abstract/9900/a_prospective,_single_arm_study_to_evaluate_the.514.aspx

Summary:

Surgical treatment of complex perianal fistula is technically challenging, associated with risk of failure, and may require multiple procedures. This study assesses the efficacy and safety of RD2-Ver.02, an autologous whole blood product created from the patients' blood, as a treatment option simple and complex transsphincteric anal fistulas.

A total of 53 patients with simple or complex transsphincteric fistulas were included in the study. MRI findings diagnosed 19 patients (36%) as simple and 34 patients (64%%) as complex AF. A total of 34 patients (69%) achieved complete healing in 6 months, while 23 out of the 34 (68%) patients with complex AF achieved complete healing in 6 months. 9 patients with perianal Crohn's disease were enrolled in the study; 6 of the 9 patients (67%) achieved complete healing in 6 months.

In this study, complete healing is defined as the absence of any anal symptom, including pain and discharge from the fistula, and a clinically confirmed closed external opening validated with a postoperative MRI. RD2 Ver.02 was found to be safe and effective in achieving healing in transsphincteric anal fistulas of both cryptoglandular and Crohn's-related origin within 6 months of treatment.

The Use Of Active Coagulation Whole Blood - An Innovative Treatment Strategy For Hard-To-Heal Wounds[15]

✎ **Author(s):** Nadav Haim, Jarrod P. Kaufman, Maxim Gurevich

✎ **Link:** https://reddressmedical.com/wp-content/uploads/2023/10/Haim-et-al-Flowable-2023.pdf

Summary:

Deep and tunneling wounds, hard-to-heal in nature, are a challenge to apply and maintain most advanced wound dressings to romote effective healing. An autologous whole blood clot is a topical treatment and has been found to be safe and effective in healing cutaneous wounds. The active coagulation whole blood (ACWB) clot treatment, using the patient's own blood, is used to treat deep and tunneling wounds, by mixing the blood with coagulation components and applying it into the wound cavity allowing the clot to re-form inside the wound.

In this study, 5 patient with multiple comorbidities, exhibiting surgical abdominal wound, chronic pilonidal sinus, stage 4 sacral pressure ulcer with exposed bone, post-amputation surgical site wound, and non-healing wound dehiscence at the site of a prior hip replacement, were all treated with the ACWB clot treatment. Complete healing was achieved in 4 out of 5 cases, demonstrating the efficacy of the ACWB treatment in deep wounds with cavaties and exposed structures. In its flowable form, the ACWB treatment safely and efficiently provides coverage of the entirety of the wound surface to improve the time and process of complex wound surface healing.

Utilization Of ActiGraft, An Autologous Whole Blood Clot, For Treatment Of Complex Wounds Linked To Comorbidities[14]

✎ **Author(s):** Emre Ozker

✎ **Link:** https://jcmimagescasereports.org/article/JCM-V3-1429.pdf

Summary:

A study was conducted to evaluate the efficacy of ActiGraft in treating complicated chronic wounds associated with various comorbidities including deep vein thrombosis post-cancer-related surgical wound, peripheral arterial disease, and Charcot foot. Severe comorbidities can have a major, negative effect on the wound healing process.

Four patients with multiple comorbidities, who failed several previous treatments, and exhibited complex wounds with exposed bone or tendon agreed to use ActiGraft. ActiGraft treatment resulted in a reduction in wound size and wound progression in a timely manner.

ActiGraft treatment was found to initiate and enhance the delayed healing process of complex and chronic wounds in patients suffering from comorbidities. ActiGraft creates a protective scaffold, restoring the homeostasis in the surrounding area of the wound, resulting in the initiation of the wound healing cascade in stagnant wounds.

Use Of Autologous Whole Blood Clot In The Treatment Of Complex Surgical Wounds: A Case Series[13]

- **Author(s):** Maxim Gurevich, Stephen Heinz, Ruhama Fridman, Chinenye Wachuku
- **Link:** https://pubmed.ncbi.nlm.nih.gov/36744737/

Summary:

A registry study of patients with surgical wounds was conducted to evaluate if an autologous blood clot, ActiGraft, can promote wound healing in complex surgical wounds.

A total of 14 patients took part in the study. Autologous whole blood clot treatment resulted in a mean percent wound area reduction of 72.33% at four weeks, with 33.33% of wounds achieving complete closure by week 4. At week 12, 78.54% of the wounds achieved complete closure. In this case series, autologous whole blood clot treatment was able to restore wound healing, avoiding the risk of infection and amputation of an affected limb. The properties of an autologous whole blood clot as an ECM reduce the risk of infection, causing the wound to progress from the inflammatory phase to the proliferative phase. Autologous whole blood clot treatment in hardto-heal surgical wounds was found to be an effective approach, reducing the risk of infection and promoting cell granulation, resulting in wound closure.

Topical Autologous Blood Clot Therapy: A Consensus Panel To Guide Use In The Treatment Of Complex Wound Types[12]

- **Author(s):** Robert Snyder, Vickie Driver, Windy Cole, Warren Joseph, Alez Reyzelman, John Lantis, Jarrod Kaufman, Terry Treadwell, Thomas Wild
- **Link: Link:** https://www.hmpgloballearningnetwork.com/site/wounds/review/topical-autologous-blood-clot-therapy-introduction-and-development-consensus

Summary:

A panel of nine clinicians from the United States and Germany with extensive experience in wound care and surgical wound management developed recommendations for topically autologous blood clot therapy (TABCT) use in specific complex wound types.

Consensus panel recommendations show TABCT application to be useful in the treatment of wounds due to its inherent properties which allow it to maintain a moist wound healing environment, assist in autolytic debridement, recruit, and deliver factors essential for conversion from a dysfunctional, inflammatory state to proliferation and wound healing, prevention of pathogen entry, and ability to completely fill non-fully visualized voids present in wounds. These abilities in addition to the cost-effectiveness, ease of access, minimal procedural and application related complications, and proven clinical efficacy of TABCT use make it a viable treatment option in the treatment of wounds in patients that cannot undergo sharp debridement, patients at high-risk for infection to occur and wound with exposed bone, tendon, undermining or tunneling.

Autologous Whole Blood Clot And Negative-Pressure Wound Therapy In South Africa: A Comparison Of The Cost And Social Considerations[11]

Author(s): Liezl Naude, Georges Balenda, Ané Lombaard

Link: Link: https://doi.org/10.7196/SAMJ.2022.v112i10.16527

Summary:

Advanced wound treatment modalities enhance healing of hard-to-heal wounds, decrease the risk of amputations, and improve the quality of life of patients. Modalities have different rates of efficacy and incur different social and financial costs to the individual and the healthcare system. This study compares the social and financial costs of using an autologous Whole Blood Clot (WBC) vs. Negative Pressure Wound Therapy (NPWT) in the treatment of diabetic foot ulcers (DFUs) in South Africa.

The cost of the autologous WBC and NPWT were compared in two scenarios: low exudate (s1) and high exudate (s2) over 4 and 12 weeks. The healing rates at 4 weeks were 19% for autologous WBC and 10% for NPWT. The autologous WBC saved 9% more in scenario 1 and 10% in scenario 2. After 12 weeks, the healing rates were 75% for autologous WBC and 43% for NPWT. The autologous WBC had a total cost savings of 43% in scenario 1 and 46% in scenario 2.

The autologous WBC consistently demonstrated better outcomes than NPWT in terms of both healing rates and cost-effectiveness.

Utilization of A Topical Autologous Blood Clot for Treatment of Pressure Ulcers[10]

Author(s): Zvi Landau, Katie Lyn Whitacre, Charles Leewood, Jessie Hawkins, Chinenye D. Wachuku

Link: https://onlinelibrary.wiley.com/doi/pdf/10.1111/iwj.13927

Summary:

Management and treatment of pressure ulcers (PUs) are met with great difficulty due to various factors that cause vulnerability of the soft tissue such as location, limited mobility, increased friction and shearing forces, as well as other comorbid-ities that may delay or halt wound healing.

This study aims to assess the efficacy of the Topically Applied Blood Clot (TABCT) in the treatment of PUs in comparison to standard of care (SOC) treatment. Twenty-four patients, 18 years or older, with PUs ranging from stage 1 to 4, were included in the study.

Efficacy in percent area reduction (PAR) on weeks 4 and 12 with TABCT over SOC was assessed. Treatment using TABCT in PUs resulted in 77.9% of the patients achieving a 50% PAR on week 4. The mean PAR on week 12 was 96.23% with 45% of the wounds treated with TABCT achieving complete wound closure. In addition, the TABCT prompted granulation tissue formation over vital structures, such as bone, which is often present in later stage PUs.

Topical Autologous Blood Clot Therapy: An Introduction and Development of Consensus Panel To Guide Use In The Treatment of Complex Wound Types[9]

- **Author(s):** Robert J. Snyder, Vickie Driver, Windy Cole, Warren S. Joseph, Alez Reyzelman, John C. Lantis II, Jarrod Kaufman, Thomas Wild
- **Link:** https://pubmed.ncbi.nlm.nih.gov/36219459/

Summary:

The complexity of a wound — whether it is acute or chronic — is based on patient-specific local, systemic, and psychosocial actors. A panel of providers experienced in wound care and surgical wound management was convened to create a series of publications on the use of topical autologous blood clot therapy (TABCT) in the treatment of complex wounds.

This publication, the first in a series, providers an evidence basis of the gap between definition and treatment of complex ounds, an overview of the use of autologous therapies in these wounds, and the science behind TABCT. In addition to this foundation of knowledge, this publication describes the plan for the consensus panel decision pathways and recommendation development of use of TABCT in the treatment of specific complex wound types.

Innovative Treatment Utilizing An Autologous Blood Clot For Diabetic Foot Ulcers[8]

- **Author(s):** Marie Williams, David Davidson, Naz Wahab, Jessie Hawkins, Chinenye Wachuku, Robert Snyder
- **Link:** https://pubmed.ncbi.nlm.nih.gov/35881826/

Summary:

Diabetic Foot Ulcer (DFU) is among the most common complications of uncontrolled diabetes. It is estimated that approximately 15% to 25% of patients with diabetes will develop a DFU in their lifetime. A DFU is a complex wound that requires considerable effort to restart a stalled healing process.

In this study, a TABCT product was used in a point-of-care setting to treat DFUs by reconstructing the extra-cellular matrix (ECM) and adjusting intricate phenotypes and mechanisms of mediators to progress towards complete healing. The TABCT product exhibited superiority over SOC treatment; 76.85% of patients achieved 50% PAR in 4 weeks, while 95% of wounds achieved complete closure in 12 weeks. By incorporating and stimulating the body's own healing capabilities into the healing process, the TABCT provided granulation over vital structures with a reduction in overall wound size in a timely manner.

Chronic Venous Ulcer Pain Reduction And Full Recovery By An Autologous Blood Clot: A Case Study[7]

- **Author(S):** Elena Dimitriou
- **Link**: www.doi.org/10.52768/2766-7820/1714

Summary:

Venous leg ulcers (VLUs) can be associated with severe pain, having a tremendous effect on the ulcer treatment and eventually the patient's life. While background pain is common in chronic wounds, dressing removal and procedures are the main cause for VLU pain.

This case study features a 63-year-old patient with a 1-year-old VLU that occured as a result of a scratch that turned into a wide-spread wound. The patient previously underwent advanced treatment with no improvement and experienced high pain levels, consuming a large amount of analgesics, ultimately, with no relief. With a weekly application of ActiGraft, the patient's pain levels progressively improved. The level of pain decreased with each application until the patient achieved complete healing after 16 weeks of treatment.

ActiGraft was found to have a significant effect in reducing wound pain levels, having an impact on the patient's wuality of life, and progresssing the hard-to-heal wound toward complete healing.

an acute wound healing trajectory significantly faster than what is suggested in the literature. Further, it is recommended that healthcare systems and insurance companies use WBC in hard-to-heal wounds to achieve complete healing and, thus, reduce the ongoing burden to the patient and associated costs.

An Observational Pilot Study To Collect Safety And Efficacy Data On Wound Care Using Whole Blood Clot Technology On Hard-To-Heal Wounds[6]

- **Author(s):** Liezl Naude; Patricia Idensohn; Febe Bruwer; Georges Balenda; Magda Mulder; Maxim Gurevich; Moreno Matityahu; Yael Izakson; Ruhama Fridman NP; Dino Rech
- **Link:** https://woundsinternational.com/journal-articles/observational-pilot-study-collect-safety-and-efficacy-data-wound-care-using-whole-blood-clot-technology-hard-heal-wounds/

Summary:

The observational pilot study demonstrates the safety and efficacy for whole blood clot (WBC) technology in a wide variety of hard-to-heal wounds.

An average of 65% reduction in patients' wound size was achieved by week 4 and 94% by week 12. In 4 of the cases described, not only did patients experience healing in hard-to-heal wounds, but scheduled amputations were avoided. Other advanced wound care therapies such as PRP, NPWT, and compression bandaging were used in 55% of patients for more than 12 months without achieving wound closure until the application of WBC. In particular, 74% of patients were previously treated with more than one NWPT dressing application without success.

These findings suggest that the application of WBC technology changes the chronic nature of the hard-to-heal wound into an acute wound healing trajectory significantly faster than what is suggested in the literature. Further, it is recommended that healthcare systems and insurance companies use WBC in hard-to-heal wounds to achieve complete healing and, thus, reduce the ongoing burden to the patient and associated costs.

Efficacy And Safety of A Novel Autologous Wound Matrix In The Management of Complicated, Chronic Wounds: A Pilot Study[5]

- **Author(s):** Igal Kushnir; Alon Kushnir; Thomas E Serena; Doron Garfinkel
- **Link**: https://pubmed.ncbi.nlm.nih.gov/27701127/

Summary:

The objective of this pilot study was to evaluate the efficacy and safety of a novel method using an autologous whole blood clot formed with the RedDress Wound Care System (RD1, RedDress Ltd, Israel), a provisional whole blood clot matrix used in the treatment of chronic wounds of various etiologies.

The pilot study demonstrated that an in-vitro blood clot using the whole blood clot matrix kit can be effectively, consistently, and safely prepared by a care provider at the point of care. The blood clot matrix was effective and safe in treating a small sample – 7 patients, 9 wounds – of patients with chronic and acute wounds that varied in severity and duration.

Complete healing, defined as complete wound closure, was achieved in 7 of the 9 wounds (78%). The 2 wounds that did not achieve complete wound closure were partially closed (Wound No. 2 was 77% closed, and wound No. 4 was 82% closed).

Safety And Efficacy Of An Autologous Blood Clot Product In The Management Of Texas 1A Or 2A Neuropathic Diabetic Foot Ulcers: A Prospective, Multicenter, Open Label Pilot Study[4]

- **Author(s):** Robert J Snyder; Maria A Kasper; Keyur Patel; Marissa J Carter; Igal Kushnir; Alon Kushnir; Thomas E Serena
- **Link:** https://pubmed.ncbi.nlm.nih.gov/29718812/

Summary:

The use of an autologous blood clot product on neuropathic DFUs was found to be safe and efficacious to use on patients with multiple, serious comorbidities. 2 of 32 adverse events (AEs) were deemed potentially device-related, however, treatment with the blood clot product continued once the AEs were resolved.

Twenty patients were enrolled in the study; 20 were analyzed in intent-to-treat (ITT) population, and 18 were in the per-protocol (PP) population. In the ITT population, 13 of 20 (65%) wounds completely healed and 13 of 18 (72.2%) PP population wounds completely healed. For purposes of the study, the efficacy of the blood product is measured as complete healing - defined as skin reepithelialization without drainage or dressing requirements confirmed at 2 consecutive study visits 2 weeks apart.

The Safety Of An Autologous Whole Blood Clot Product Applied To Full Thickness Dermal Wounds in A Porcine Model For Up To 18 Days[3]

Author(s): Igal Kushnir; Alon Kushnir; Thomas E Serena; Raphael A Yaakov; Kristen A Eckert

Link: https://doi.org/10.2147/CWCMR.S189836

Summary:

Blood has become a major source for wound care products due to its primary role in wound healing. In this study, the safety of an autologous whole blood clot product was evaluated in porcine models. The blood clot provides a fibrin scaffold that serves as a protective, provisional extracellular matrix. The clot dries out and becomes a protective scab, under which a moist wound environment can be maintained.

The use of the autologous whole blood clot product applied to full thickness dermal wounds in a porcine model proved to be a beneficial treatment for acute full-thickness wounds. Three of the four pigs in the model-study were allocated to the whole blood clot product intervention group, whereas 1 was allocated to the control. By the 18th — and final — day, the wound area of the intervention group reduced by 66%, compared to the control (41%).

Microscopic evaluation of the wounds indicated that the whole blood clot product achieved partial-to-complete wound reepithelialization, whereas only minimal reepithelialization was present in the control.

Proposed Mechanism Of Action Of Topically Applied Autologous Blood Clot Tissue: A Quintessential Cellular And Tissue Based Therapy[2]

Author(s): Robert J Snyder; Gregroy Schultz; Chinenye Wachuku; Arij M Rashid; J. Karim Karim Ead

Link: https://doi.org/10.7547/20-140

Summary:

The topically applied autologous blood clot tissue creates a scaffold that serves as a biologic delivery system that functions to control the release of growth factors and cytokines.

Activated platelets and fibrin set forth the groundwork of the scaffold via conformational change and cleavage. Platelets provide immunity to the wound site, aid in the inflammatory process, and provide essential growth and clotting factors that are essential in wound healing; while the fibrin matrix provides a temporary ECM, aids in issue repair, leukocyte adhesions, endothelial cell migration during angiogenesis, and recruits cells to trigger fibrin-mediated responses.

Topically applied blood clot tissue can lower bacterial bioburden while stimulating angiogenesis and fostering the movement of keratinocytes and fibroblasts.

Use Of An Autologous Matrix On Diabetic Foot Ulcers With Near-Infrared Spectroscopy And pH Measurement[1]

Author(s): Leticia Vallejo; Jean Achterberg

Link: https://pubmed.ncbi.nlm.nih.gov/33249991/

Summary:

The study aims to evaluate the efficiency of an autologous whole blood clot (WBC) matrix on diabetic foot ulcers (DFU), and analyse its immune response with near-infrared spectroscopy (NIRS) and pH measurement.

The use of an autologous matrix was effective in healing three non-healing DFUs. Quantitative measurements taken with the NIRS indicated:

- An increase in StO2%, HbO2, and tHb and a decrease in Hb
- An increase in angiogenesis in the local wound area tissue

Wound-size reduction was 70% after two applications, 97.6% after three applications, and 90.9% after four applications. The NIRS skeletal muscle oxygen saturation (StO2) increased in all cases. Overall, the autologous matrix was effective in improving the qualitative aspects of the treated wounds, as well as the course of the wound healing process, as measured by PAR, oxygen saturation values, and local pH levels.

Scientific Publications

Utilization Of ActiGraft, An Autologous (Blood Clot) Graft In The Reconstruction Of Soft Tissue Deficit From Hand Trauma – A Case Study[4]

Author(s): Richard D Curtis; Chinenye D Wachuku

Link: https://juniperpublishers.com/arr/pdf/ARR.MS.ID.555692.pdf

Summary:

This case study found ActiGraft to be a safe and effective wound treatment which showed to be successful in treating a deep cutaneous injury on the patient's hand. ActiGraft not only successfully repaired the skin deficit, but simultaneously mitigated scar formation while supporting good hand mobility.

Data demonstrated a decrease in wound size by 73% after a single application. By week 5, the fourth and final ActiGraft treatment was applied to the wound which consisted of healthy granulated tissue and no longer exhibited any fibrotic or necrotic tissue, as well as no presence of slough. Complete wound healing was achieved on week 10 post-surgical with minimal scar formation, a challenging concern.

Scar formation is a challenging concern that has brought about immense clinical and financial burden on the healthcare system. The ActiGraft treatment was found to be cost-effective in comparison to alternative treatments; the cost of ActiGraft is more than 50% less than some other wound treatments for the equivalent time period of use. ActiGraft showed high efficacy in healing complex and deteriorating wounds with the potential to dramatically reduce the financial cost on the health system.

The Use Of ActiGraft, An Autologous Skin Graft, In The Treatment Of Complex Diabetes Foot Ulcer[3]

Author(s): Emre Ozker; Chinenye Wachuku Meng

Link: https://juniperpublishers.com/arr/pdf/ARR.MS.ID.555685.pdf

Summary:

This case study found ActiGraft to be a highly effective and cost-efficient wound care solution for treating chronic diabetic foot ulcers (DFUs). DFUs are a complication associated with many comorbidities that can result in long-term hospitalization, limb amputation, and even death. ActiGraft proved successful in treating a hard-to-heal, chronic DFU that presented extensive necrotic tissue, after multiple other wound treatments failed. ActiGraft creates a fibrin clot using the patient's own blood which minimizes concerns of possible adverse reactions and further complications while promoting the natural healing process of the wound.

After only three weeks of use, the ActiGraft treatment demonstrated rapid tissue granulation growth over the exposed bone, tendons and fascia, with reduction in size of the wound area. Furthermore, the weekly application of ActiGraft demonstrated the importance of wound bed preparation by achieving tissue management, inflammation and infection control, moisture balance, and epithelial edge advancement.

These findings highlight the safety and efficacy of the cutting-edge technology harnessed in the ActiGraft product and bring an in-depth discussion to ActiGraft's success in healing chronic DFUs.

ActiGraft Treatment In Complex Wounds With Exposed Structure - A Case Series[2]

Author(s): Maxim Gurevich, Naz Wahab, Chinenye Wachuku, Karim Ead J, Robert J Snyder

Link: https://juniperpublishers.com/arr/pdf/ARR.MS.ID.555701.pdf

Summary:

Limb amputations as a result of non-healing complex wounds continues to be with high prevalence. A non-healing wound can deteriorate and have an extensive breakdown of soft tissue that may cause exposure of vital structures. In complex wounds with exposed structures, ActiGraft proved to:

- Achieve coverage of these vital structures and reduction in the wound area, notwithstanding multiple previous treatments that failed to progress the wound.
- Be applied in an outpatient setting, preventing the need for hospital admission which has significant positive impact on the health economics of wound care globally.

In the study, it was indicated that achieving closure of the wound by enhancing the body's physiological means links to the demonstrated high safety pattern of the ActiGraft treatment.

ActiGraft Topically Applied Blood Clot Therapy[1]

Author(s): Robert Snyder

Link: https://podiatrym.com/Clinical_Innovations2.cfm?id=2807

Summary:

ActiGraft is a topically applied blood clot therapy supported by evidence of efficacy in treating foot ucler patients with diabetes.

There are 34.2 million patients with diabetes in the United States with foot ulcers considered one of the most common complications of diabetes. Complex ulcerations with exposed tendon and bone pose the greatest risk od osteomyelitis. owever, most studies regarding ulcer healing in this group include full thickness wounds with a paucity of evidence surrounding complex ulcerations. Performing randomized controlled trials on complex DFUs represents an unmet clinical need.

In this study, three sites are planning and will be overseen by key opinion leadsers in the wound research field. A multicenter, prospective randomized controlled trial will occur in three stages. The proposed study will address therapeutic efficacy of this treatment in deleterious circumstances and will include a standard of care control arm.

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Scientific Publications

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[3] Emre O, Chinenye W M. The Use of ActiGraft, an Autologous Skin Graft, in the Treatment of Complex Diabetes Foot Ulcer - A Case Study. Ann Rev Resear. 2021; 6(2): 555685.DOI: 10.19080/ARR.2021.06.555685

[2] Gurevich, M., Wahab, N., Wachuku, C., Ead J, K., & Snyder, R. J. (2021). ActiGraft Treatment in Complex Wounds with Exposed Structure - A Case Series. Juniper Publishers, 7(1).

[1] Snyder, R. ActiGraft Topically Applied Blood Clot Therapy. Podiatry Management: Clinical Innovations/The Diabetic Foot. (2021).

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REVOLUTIONIZING **WOUND TREATMENT**

Legacy Medical is committed to improving the health and lives of patients around the world by revolutionizing the way we treat hard-to-treat wounds. Our innovative products are advanced, biologic wound care solutions that recreate the natural wound healing processes of the body.

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APPENDIX A: ActiGraft^{PRO} System Components

The ActiGraft^{PRO} System provides single-use components needed for the safe and rapid preparation of Whole Blood Clot (WBC) gel from a small sample of a patient's own peripheral blood. Each system is comprised of an individual box that contains all the components needed to prepare an ActiGraft^{PRO} whole blood clot.

SKU: RD2301

Patient Phlebotomy System:

- Gauze pad
- ACD-A tube
- Bandage
- 18" Tourniquet
- Needless blood transfer set
- Alcohol Pad
- Blood draw needle

Coagulation & Accelerator System:

- Clotting blister containing kaolin powder and calcium gluconate powder
- Syringe and adapter

System Accessories:

- Gloves
- Drape
- Gauze
- Steri-strip
- Non adherent dressing
- Hydrophilic Foam Dressing
- Face mask with eye protection
- Tape, Ø .5" circle band-aid
- Puncture tool

APPENDIX B: Case Studies

CASE STUDY: LOWER EXTREMITY WOUND

- **100% WOUND REDUCTION**
- **TOTAL HEALING IN 8 WEEKS**
- **5 ACTIGRAFT APPLICATION**

PATIENT: 68 year-old, female

PMH: Diabetic, Peripheral Vascular Disease

WOUND PROPERTIES:

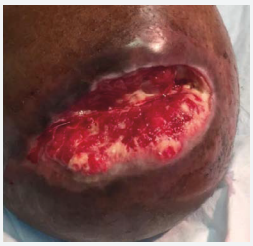
- Below the knee amputation (left leg) with failure to muscle flap
- Original wound divided into 2 wounds due to epithelial bridge that separated the original wound

PAST TREATMENTS: Surgical Debridement, NPWT, HBO

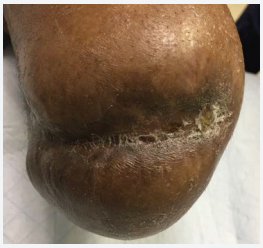
OFFLOADING: Wheelchair Bound

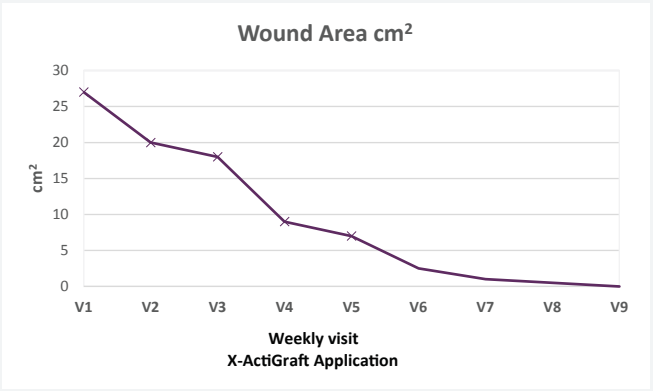
ACTIGRAFT TREATMENT PROGRESSION:

Day 0



Day 63





CASE STUDY: LOWER EXTREMITY WOUND

- **100% WOUND REDUCTION**
- **TOTAL HEALING IN 15 WEEKS**
- **10 ACTIGRAFT APPLICATIONS**

PATIENT: 69 year-old, male

PMH: Diabetic Mellitus Type 2

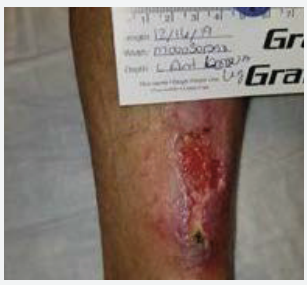
WOUND PROPERTIES:

- MRSA infection treated with Doxycycline

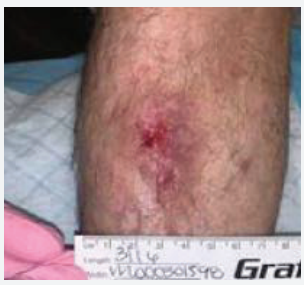
PAST TREATMENTS: Ultra-MIST treatment and topical European Wound Gel, Allicin

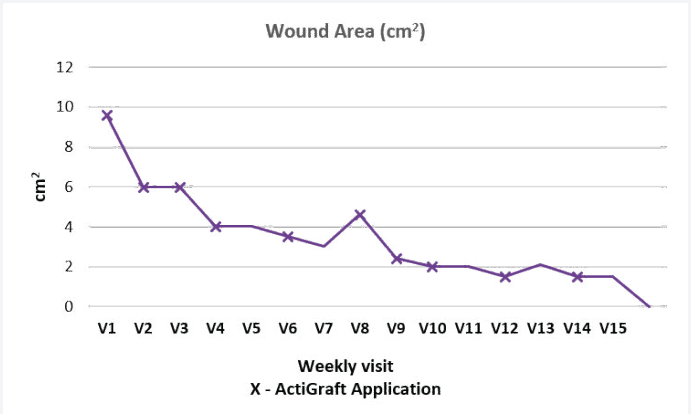
ACTIGRAFT TREATMENT PROGRESSION:

Day 0



Day 91





CASE STUDY: VENOUS LEG ULCER

- **98% WOUND REDUCTION**
- **TOTAL HEALING IN 17 WEEKS**
- **16 ACTIGRAFT APPLICATIONS**

PATIENT: 87 year-old, male

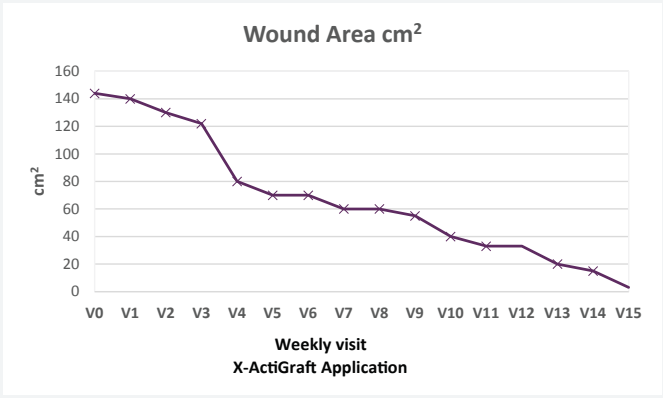
PMH: Venous Insufficiency, controlled diabetes type 2, hypertension

WOUND PROPERTIES:

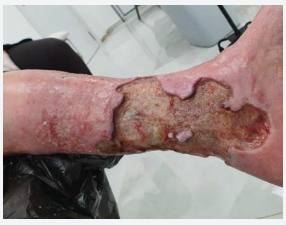
- VLU on calf and shin, heavy exudating

PAST TREATMENTS: Ozone gas treatment for 4 years- deterioration Advanced wound dressings for the last 2 years

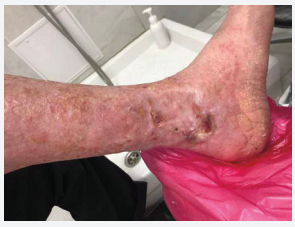
ACTIGRAFT TREATMENT PROGRESSION:



Week 1



Week 17



CASE STUDY: DIABETIC FOOT ULCER

- **99% WOUND REDUCTION**
- **2 ACTIGRAFT APPLICATIONS**

PATIENT: 60 year-old, male

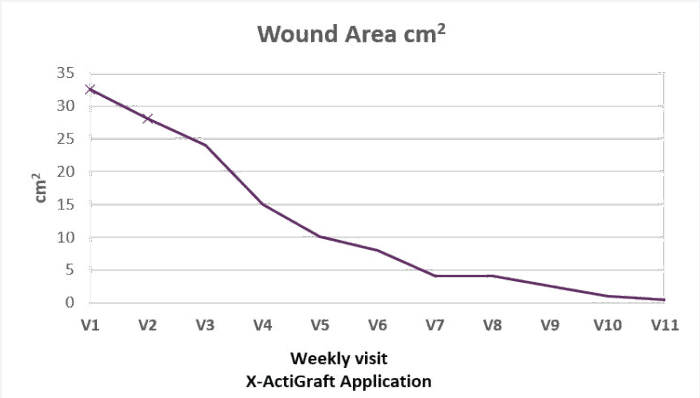
PMH: T2DM, Chronic Osteomyelitis

WOUND PROPERTIES:

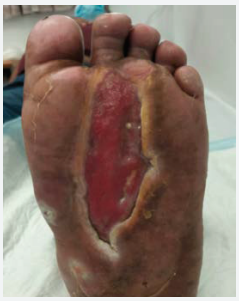
- Plantar DFU with chronic osteomyelitis of ray 1 in the affected foot

PAST TREATMENTS: NPWT, advanced dressings

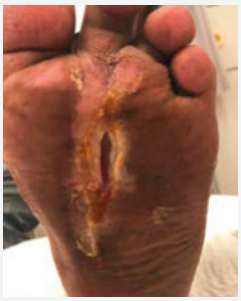
ACTIGRAFT TREATMENT PROGRESSION:



Day 1



Day 71



Explore our case study library to see how we are healing wounds, visit: **reddressmedical.com/case-studies/**

APPENDIX C: Technical Specifications

INTENDED USE

ActiGraft[PRO] is intended to be used at point-of-care for the safe and rapid preparation of WBC gel from a small sample of a patient's own peripheral blood. Under the supervision of a healthcare professional, the WBC gel produced by the ActiGraft[PRO] is topically applied for the management of exuding cutaneous wounds, such as leg ulcers, pressure injuries, diabetic ulcers, and mechanically or surgically-debrided wounds. Prescription use only.

- Clot size: 28.3 sq.cm.
- Diameter: 6 cm
- 18ml of blood required
- Shelf life: 2 years (according to labels)

Storage conditions - Store in the original container at a room temperature of 5°C (41°F) – 30°C (86°F). Protect from freezing and avoid excessive heat.

USE OF THE SYSTEM

ActiGraft[PRO] should be used in conjunction with standard of care procedures for comprehensive wound management such as:

- Removal of necrotic or infected tissue
- Off-loading
- Compression therapy for venous stasis ulcers
- Establishment of adequate blood circulation
- Management of wound infection
- Management of underlying disease
- Wound cleansing
- Nutritional support, blood glucose control for subjects with diabetic ulcers
- Bowel/bladder care for subjects with pressure injuries at risk for contamination

CONTRAINDICATIONS

ActiGraft[PRO] is contraindicated in patients with the following types of wounds:

- Wounds due to malignancy
- Untreated osteomyelitis
- Wounds with active clinically diagnosed infection

PRECAUTIONS

- Some blood-contacting components of ActiGraft[PRO] have been sterilized by Ethylene Oxide, which can cause serious allergic reactions in some sensitized individuals.
- Throughout the processing and application of ActiGraft[PRO], use universal precautions as defined by the facility policy and procedure manual. All parts of the procedure shall be performed in such a manner as to minimize splashing, spattering, and generation of potential droplets.
- Calcium gluconate powder should only be used with ActiGraft[PRO] System.

View safety information here: www.legacymedicalconsultants.com/actigraft-safety-info

APPENDIX D: W-9

Form **W-9**
(Rev. October 2018)
Department of the Treasury
Internal Revenue Service

Request for Taxpayer Identification Number and Certification

▶ Go to *www.irs.gov/FormW9* for instructions and the latest information.

Give Form to the requester. Do not send to the IRS.

Print or type. See Specific Instructions on page 3.

1 Name (as shown on your income tax return). Name is required on this line; do not leave this line blank.

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2 Business name/disregarded entity name, if different from above

3 Check appropriate box for federal tax classification of the person whose name is entered on line 1. Check only **one** of the following seven boxes.

☐ Individual/sole proprietor or single-member LLC ☐ C Corporation ☐ S Corporation ☑ Partnership ☐ Trust/estate

☐ Limited liability company. Enter the tax classification (C=C corporation, S=S corporation, P=Partnership) ▶ _____

Note: Check the appropriate box in the line above for the tax classification of the single-member owner. Do not check LLC if the LLC is classified as a single-member LLC that is disregarded from the owner unless the owner of the LLC is another LLC that is **not** disregarded from the owner for U.S. federal tax purposes. Otherwise, a single-member LLC that is disregarded from the owner should check the appropriate box for the tax classification of its owner.

☐ Other (see instructions) ▶

4 Exemptions (codes apply only to certain entities, not individuals; see instructions on page 3):

Exempt payee code (if any) _____

Exemption from FATCA reporting code (if any) _____

(Applies to accounts maintained outside the U.S.)

5 Address (number, street, and apt. or suite no.) See instructions.

9800 Hillwood Pkwy Ste 320

Requester's name and address (optional)

6 City, state, and ZIP code

Fort Worth TX 76177

7 List account number(s) here (optional)

Part I Taxpayer Identification Number (TIN)

Enter your TIN in the appropriate box. The TIN provided must match the name given on line 1 to avoid backup withholding. For individuals, this is generally your social security number (SSN). However, for a resident alien, sole proprietor, or disregarded entity, see the instructions for Part I, later. For other entities, it is your employer identification number (EIN). If you do not have a number, see *How to get a TIN,* later.

Note: If the account is in more than one name, see the instructions for line 1. Also see *What Name and Number To Give the Requester* for guidelines on whose number to enter.

Social security number

			–			–				

or

Employer identification number

8	4	–	3	2	6	5	3	7	0

Part II Certification

Under penalties of perjury, I certify that:

1. The number shown on this form is my correct taxpayer identification number (or I am waiting for a number to be issued to me); and
2. I am not subject to backup withholding because: (a) I am exempt from backup withholding, or (b) I have not been notified by the Internal Revenue Service (IRS) that I am subject to backup withholding as a result of a failure to report all interest or dividends, or (c) the IRS has notified me that I am no longer subject to backup withholding; and
3. I am a U.S. citizen or other U.S. person (defined below); and
4. The FATCA code(s) entered on this form (if any) indicating that I am exempt from FATCA reporting is correct.

Certification instructions. You must cross out item 2 above if you have been notified by the IRS that you are currently subject to backup withholding because you have failed to report all interest and dividends on your tax return. For real estate transactions, item 2 does not apply. For mortgage interest paid, acquisition or abandonment of secured property, cancellation of debt, contributions to an individual retirement arrangement (IRA), and generally, payments other than interest and dividends, you are not required to sign the certification, but you must provide your correct TIN. See the instructions for Part II, later.

Sign Here **Signature of U.S. person ▶** [signature] **Date ▶** 4-1-2022

General Instructions

Section references are to the Internal Revenue Code unless otherwise noted.

Future developments. For the latest information about developments related to Form W-9 and its instructions, such as legislation enacted after they were published, go to *www.irs.gov/FormW9.*

Purpose of Form

An individual or entity (Form W-9 requester) who is required to file an information return with the IRS must obtain your correct taxpayer identification number (TIN) which may be your social security number (SSN), individual taxpayer identification number (ITIN), adoption taxpayer identification number (ATIN), or employer identification number (EIN), to report on an information return the amount paid to you, or other amount reportable on an information return. Examples of information returns include, but are not limited to, the following.

- Form 1099-INT (interest earned or paid)
- Form 1099-DIV (dividends, including those from stocks or mutual funds)
- Form 1099-MISC (various types of income, prizes, awards, or gross proceeds)
- Form 1099-B (stock or mutual fund sales and certain other transactions by brokers)
- Form 1099-S (proceeds from real estate transactions)
- Form 1099-K (merchant card and third party network transactions)
- Form 1098 (home mortgage interest), 1098-E (student loan interest), 1098-T (tuition)
- Form 1099-C (canceled debt)
- Form 1099-A (acquisition or abandonment of secured property)

Use Form W-9 only if you are a U.S. person (including a resident alien), to provide your correct TIN.

If you do not return Form W-9 to the requester with a TIN, you might be subject to backup withholding. See What is backup withholding, *later.*

Cat. No. 10231X Form **W-9** (Rev. 10-2018)

APPENDIX E: Reimbursement

Sources:

*Medicare NCD 270.3 NCD - Blood-Derived Products for Chronic Non-Healing Wounds (270.3) (cms.gov) HCPCS
*July 2023 Quarterly Update CMS HCPCS Quarterly Update | CMS
*2024 ICD-10-CM Expert for Hospitals Optum 360, LLC
*Medicare Claims Processing Manual 100.04 Chapter 32 Section 11.3.2: Medicare Claims Processing Manual (cms.gov)
*National Coverage Determination (NCD) 270.3 Blood-Derived Products for Chronic, Non -Healing Wounds
*MedLearn Matters CR Number 12403 Effective Date April 13, 2021
*MM12403 - National Coverage Determination (NCD) 270.3 Blood-Derived Products for Chronic, Non-Healing Wounds (cms.gov)

*Calendar Year 2024 Medicare Outpatient Prospective Payment System, Final Rule (CMS-1786-FC), Federal Register, November 22 , 2023 Addenda B and D
*CY 2024 National Physician Fee Schedule Relative Value File January Release, January 1, 2024
*2024 HCPCS Level II Expert AAPC

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APPENDIX F: Citation List

[1]Donner, B, et al. Analysis of Three Prospective, Open-Label, Clinical Trials with Autologous Blood Clot in Chronic Wounds.

[2]Boulton AJM, The Diabetic Foot, Medicine 43:1 2014

[3]Stadler L, Wound Debridement – Robust Growth in a Dynamic Market, SmartTRAK 2018.

[4]Prompers L et al, Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and with-out peripheral arterial disease, Diabetologia, 2008; 51(5).

[5]P. (2019, September). Surgical site infections. Retrieved February, from https://psnet.ahrq.gov/primer/surgical-site-infections

[6]King, K. (2018, August 28). A critical look at readmissions for patients with diabetic foot infections. Retrieved February 12, 2021, from https://www.podiatrytoday.com/critical-look-readmissions-patients-diabetic-foot-infections

[7]Stevens P, The Cost of Diabetic Foot Ulcers, The O&P Edge, August 2015, seen 19 March 2019 in https://opedge.com/Articles/ViewArti-cle/2015-08_02.

[8]Järbrink K et al, The humanistic and economic burden of chronic wounds: a protocol for a systematic review, Systematic Reviews 6:15 2017.

[9]Snyder RJ, Schultz G, Wachuku C, Rashid AM, Ead JKK. Proposed Mechanism of Action of Topically Applied Autologous Blood Clot Tissue: A Quintessential Cellular and Tissue Based Therapy. J Am Podiatr Med Assoc. 2020 Oct 13:20-140. doi: 10.7547/20-140. Epub ahead of print. PMID: 33052392.

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