

الأساليب الحديثة في علاج الجروح المزمنة (الطباعة الحيوية للأنسجة ثلاثية و رباعية الأبعاد)

الدكتورة نورا سالم سلمان مرزوق
ماجستير في تعليم المهن الصحية
البورد الأمريكي في الطب التجميلي ومكافحة الشيخوخة
الجراحة التجميلية، طبيب تجميلي ودولي متخصص في
العناية بالجروح
رئيس مركز التطوير المهني المستمر والطب التجديدي
مدرب دولي للطباعة الحيوية للأنسجة الرباعية و الليزر
عضو هيئة التدريس ومنسق المقررات الدراسية في
جامعة الشارقة

اهداف المحاضرة

1- عرض الخدمات الحديثة المتوفرة حول علاج الأنسجة و الجروح المزمنة

2- لتوضيح آلة الطباعة الحيوية للأنسجة ثلاثية الأبعاد في علاج الجروح المزمنة

3- مشروع تحسين جودة المنشأة الطبية

4- مشاركة بعض الحالات للطباعة الثلاثية و رباعية الأبعاد

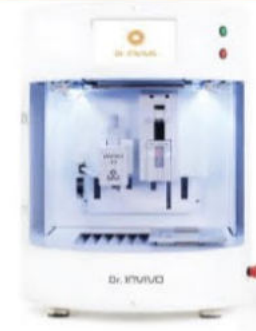
تكنولوجيا الطباعة ثلاثية و رباعية الأبعاد

BUSINESS MODEL

DFUREGEN KIT: 1 KIT PER PATIENT



DR.INVIVO DFU



KEY PARTNER



BLUE OCEAN MARKET

- No Regulatory Barriers
- EMA Classification: "Non-ATMPs"
- Autologous & Homologous Use
- Considered as "Same Surgical Procedure"

PATENTED TECHNOLOGY

- High Barriers to Entry
- Patents & Certification Protection
- Consolidated Organ Regeneration Platform
- CoE Establishment for Training & Seminars

BENEFITS OF PARTNERING

- High Return, Zero Competition
- No Additional Drug Wholesaler
- Reliable Business Partner
- Maximum Gross Margin (50%)



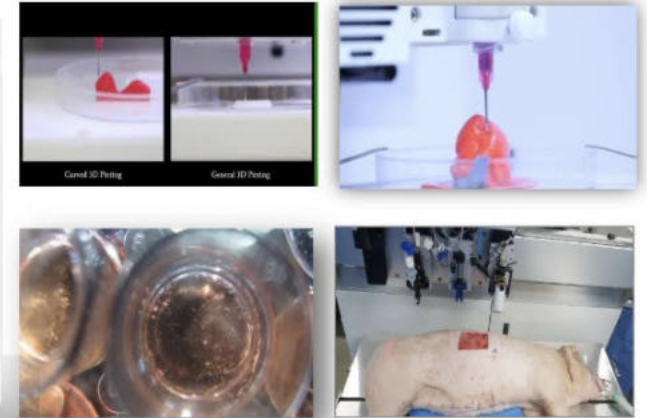
Dr. INVIVO 406



تكنولوجيا الطباعة رباعية الأبعاد



✓ ROKIT developed 4D organ regenerator, Dr.INVIVO making possible customizing healthcare solution.



**في إطار خطط وبرامج الوزارة لإحداث التحول في مجال الرعاية الصحية
المقدمة للمرضى**

**توفير أحدث الطرق العلاجية، وتقديم خدمات صحية متخصصة شاملة
ومبتكرة بمعايير عالمية**

**1. تهدف إلى تحقيق أهداف عام الاستعداد للخمسين تماشياً مع مئوية
الإمارات 2071**

**2. إجراء أول عملية من نوعها في المنطقة على يد فريق طبي إماراتي
التيكولوجيا هي ثورة علمية في الطب الحيوي الجديد**

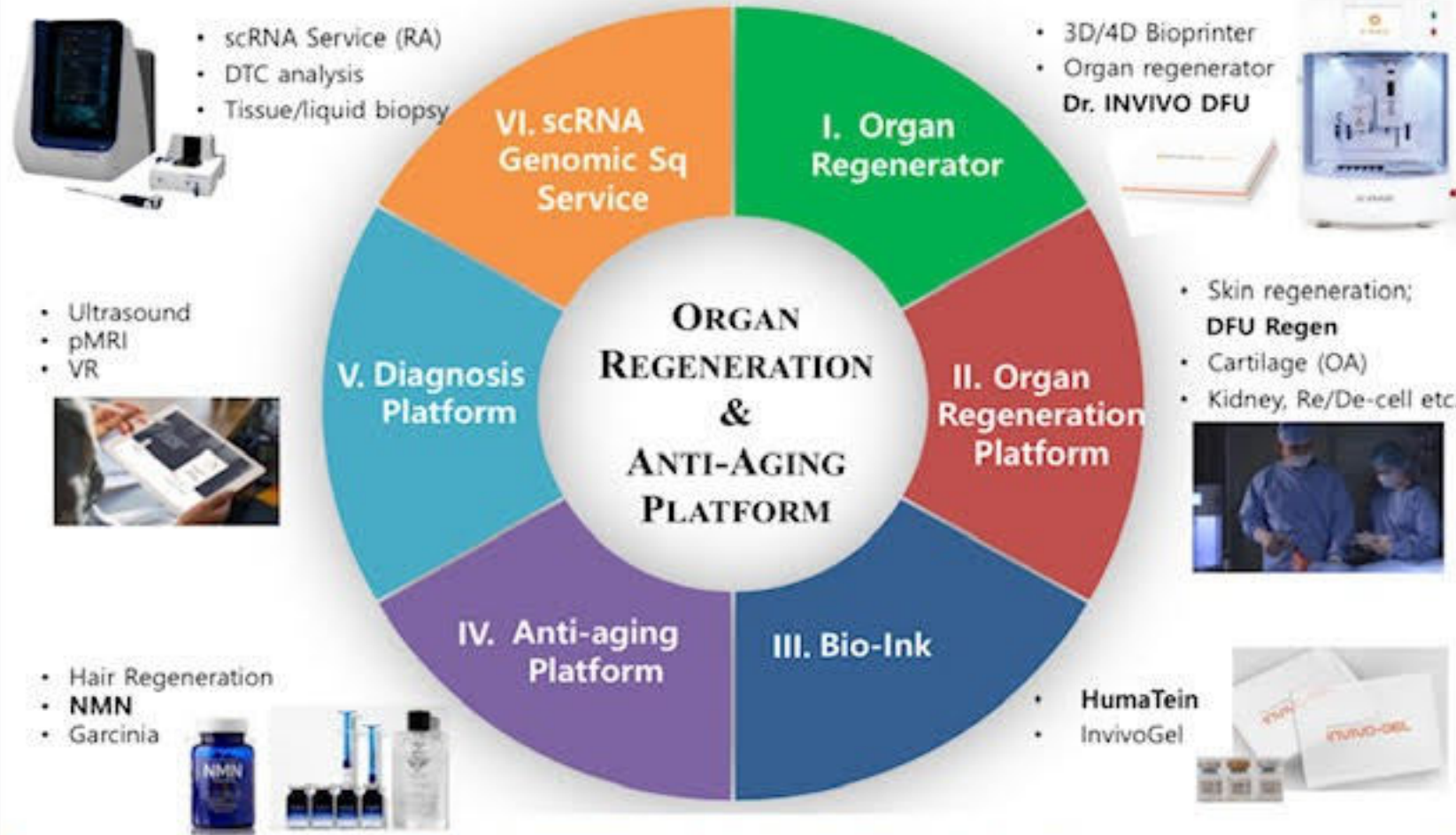
**3. يمهد الطريق لعصر جديد في علاج مرضى القدم السكرية المزمنة
4. الجروح والحروق**

**5. الوزارة تطلق أول مركز امتياز لتدريب الأطباء على أحدث تكنولوجيات
جديدة**

6. مدة العملية 45 دقيقة (جراحة اليوم الواحد)

TOTAL SOLUTION FOR AGING RELATED CHRONIC DISEASE

ROKIT's Destructive Innovation Healthcare Platform for Chronic & Complicated Disease

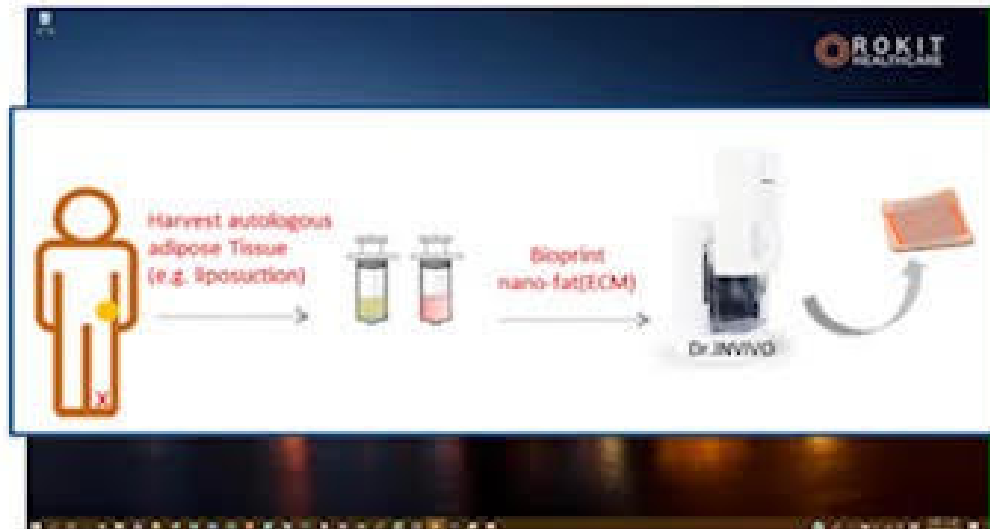


- 1- عملية الطباعة باستخدام الادهون ثلاثية (شفت الادهون 80-100 مل)
- 2- استخدام الخدير الموضعي واستخدام الادهن كحبر لطباعة الطعوم البيولوجية
- 3- إضافة مواد بيولوجية تعمل كنوع من الغراء حتى تتمكن من الالتصاق بالجسم
- 4- المكان المراد علاجه (الجروح المفتوحة والحروق وتقرحات القدم السكرية)
- 5- العملية تستغرق 45 دقيقة المساعة
- 6- تتم الطباعة في بيئة معقمة حتىلا تموت الخلايا البشرية



DIABETIC FOOT REGENERATION THERAPY

DFURegen, autologous customizing therapeutic solution with 4D bioprinting technology



كيف تم اكتشاف التكنولوجيا واختيارها؟

هذه التقنية متاحة في العالم منذ عام 2012 ولكنها كانت تلجأ فقط -
واعتمد عليها الأطباء كأداة تشخيصية وتخصيص العلاج



لماذا تم اختيار هذا المشروع؟

خطورة بعض الحالات :مثل الجروح المزمنة والحروق تقرحات الفراش
وقروح القدم التي يمكن ان تزيد من معدلات الوفيات

التكلفة الباهظة: زيادة الإقامة في المستشفى، والضمادات اليومية،
والإجراءات الجراحية المتعددة، ومعدلات الرفض وإعادة القبول

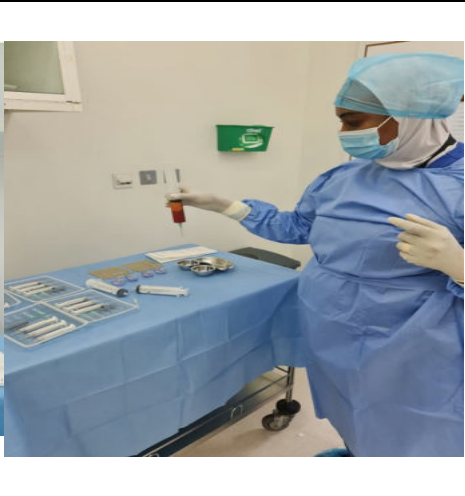
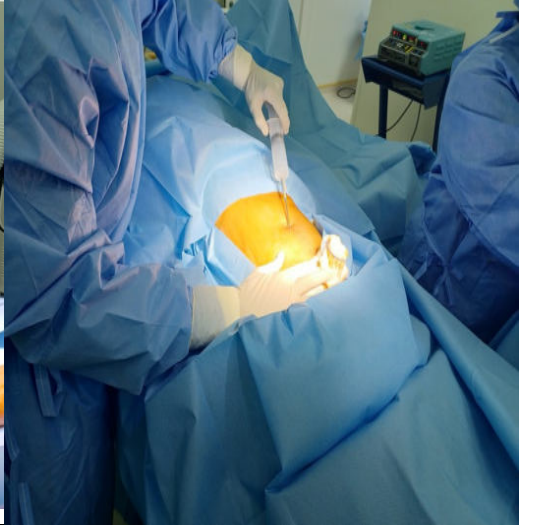
ترتبط حالات الاستشفاء الممتدة هذه بارتفاع التكاليف وزيادة حالات
العدوى و/أو المضاعفات الأخرى

استياء المريض والأسرة: يؤدي إلى آلام المرضى ومعاناتهم وعواقب
وخيمة. يُظهر المرضى ضعفًا كبيرًا في الوظيفة البدنية والاجتماعية
والرعاية الذاتية والتنقل

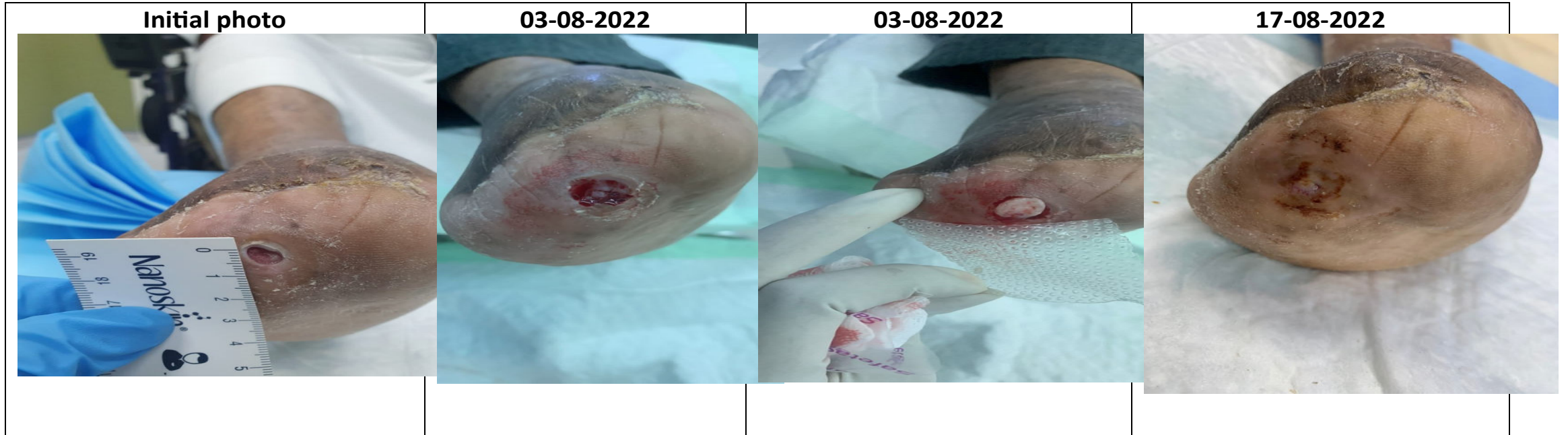
الأثر الإيجابي من هذه الخدمة

:الفرق بين التقنية والتقنيات الأخرى المستخدمة لنفس الحالات كما يلي

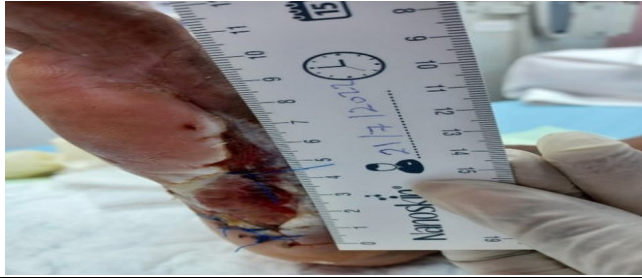
- أ) لا يتطلب دخول أي مريض إلى المستشفى بعد العملية
- ب) لن يستغرق الإجراء بأكمله سوى 45 دقيقة وأقل
- ج) لا يوجد رفض من الجسم أو أي حساسية
- د) يأتي معدل الاسترداد أسرع بنسبة 80% على الأقل من الطرق الأخرى مثل وقت الاسترداد
- هـ) التكلفة قابلة للمقارنة بالطرق الأخرى الأقل



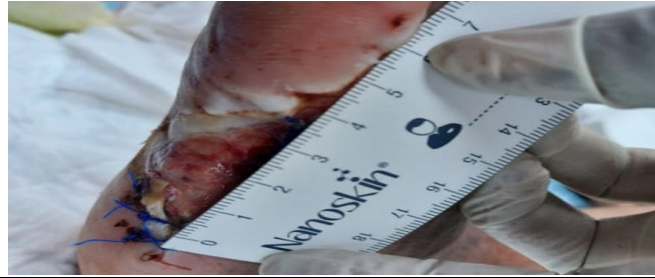
حالة قدم سكرية لسنوات من المعاناة



Initial photo



Initial photo

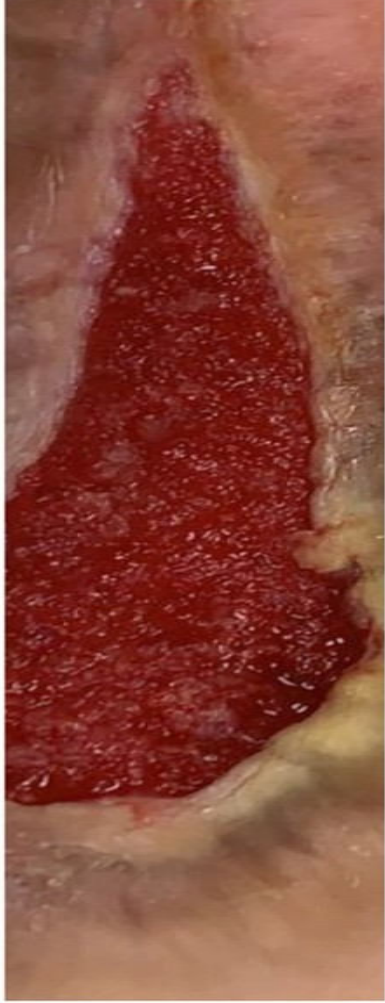


**OT day
Pre debridement**

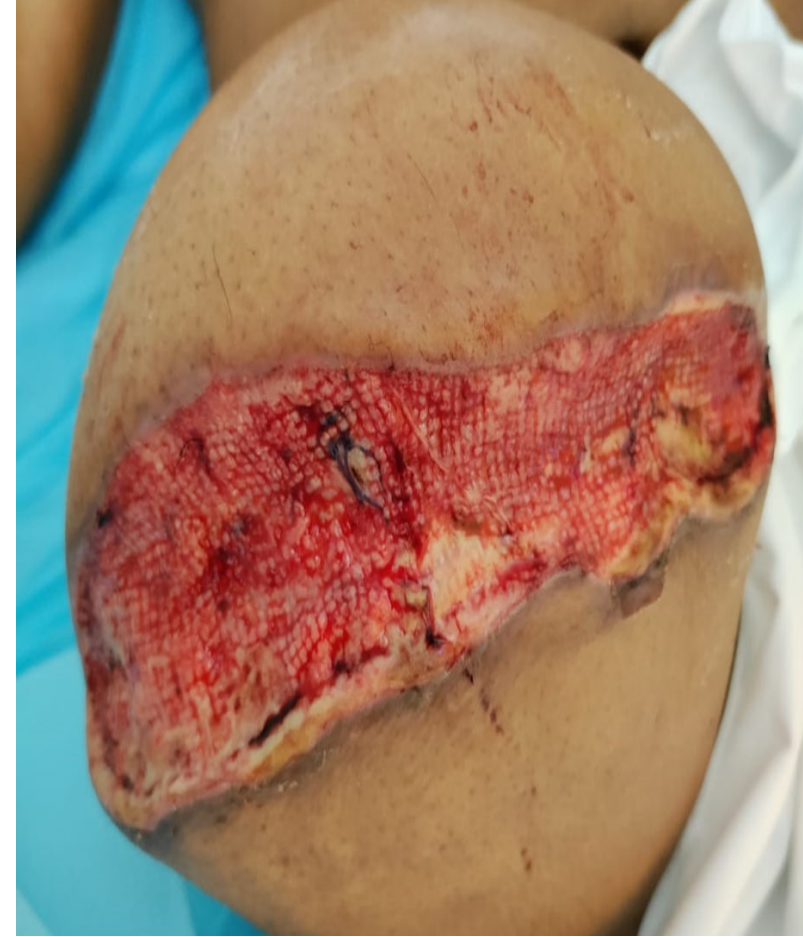


**OT day
Post debridement**





حالة اخرى لبتر قدم سكرية

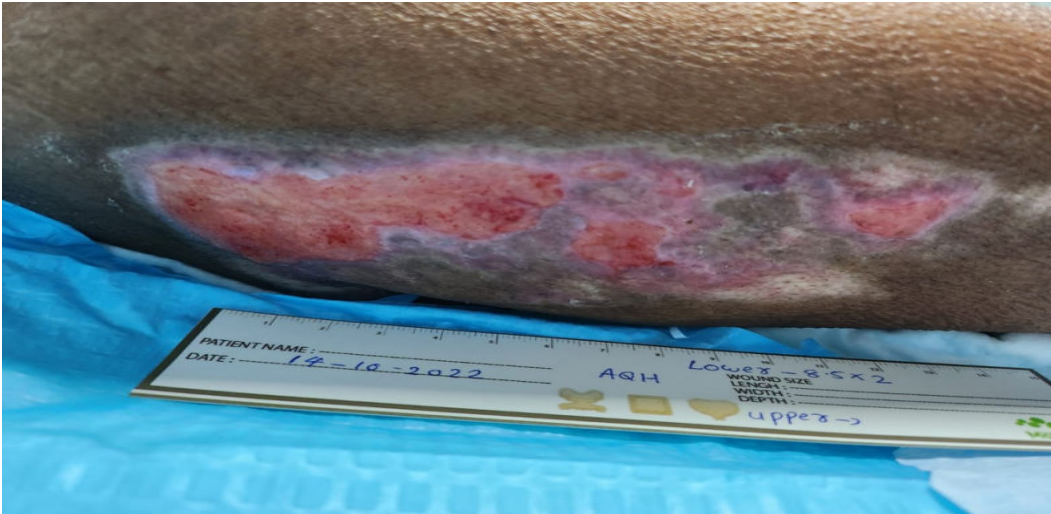
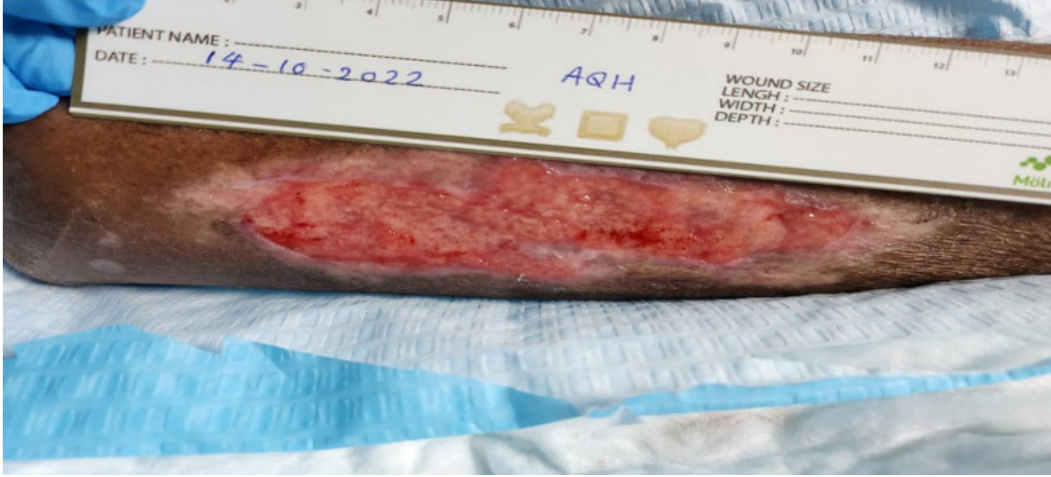




حالة حروق من الدرجة الثانية العميقة



حالة حروق من الدرجة الثانية العميقة وشفاء تام



CLINICAL TRIAL IN INDIA; The manuscript has been published to *Gels*. (Impact Factor: 3.96)

New Paradigm in Diabetic Foot Ulcer Grafting Techniques using 3D Bioprinted Autologous Minimally Manipulated Homologous Adipose Tissue (3D-AMHAT): A Pilot Study

Dr. Mohd Yazid Bajuri | Jeehee Kim

ABSTRACT

Background: Adipose tissue is an abundant source of extracellular substances that supports the tissue repair process. This pilot study is to determine the efficacy of 3D bioprinted autologous adipose tissue graft on diabetic foot ulcers (DFUs).

Methods: Single arm, pilot study in Diabetic Foot Services clinic. Ten patients with a DFU were enrolled from August 2021 to November 2021. The primary endpoint was the complete healing within 12 weeks. The secondary end points were wound size reduction, time to healing, and adverse events.

Results: 7 out of 10 patients showed complete healing of DFU within 12 weeks (at 2, 4, 5, 10, and 12 weeks, respectively).

The wound size reduction rate was significantly and progressively reduced over time.

Conclusion: Our data suggest that autologous adipose tissue grafting using the 3D bioprinter promotes wound healing with high-quality skin reconstruction. There were no adverse events.

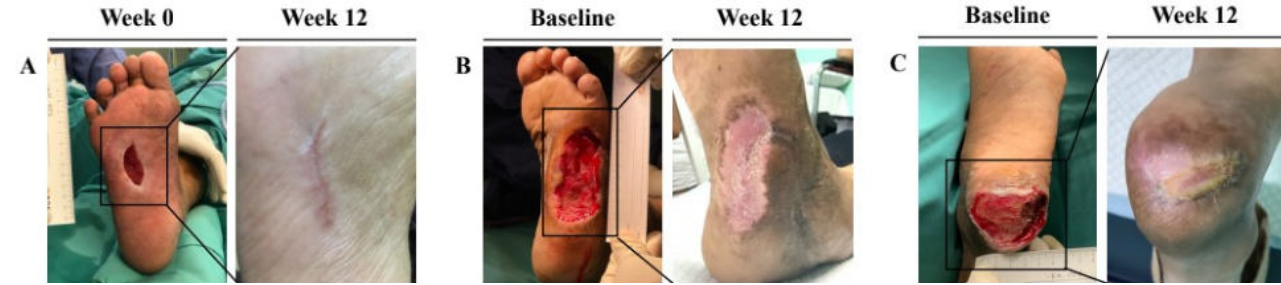


Figure 1. Complete wound healing outcome among the patients with diabetic foot ulcer. A – C) Complete healing of 4 patients within 12 weeks. Black squares at week 0 indicated the ulcer before the treatment. Complete wound healing images at week 12 were magnified.

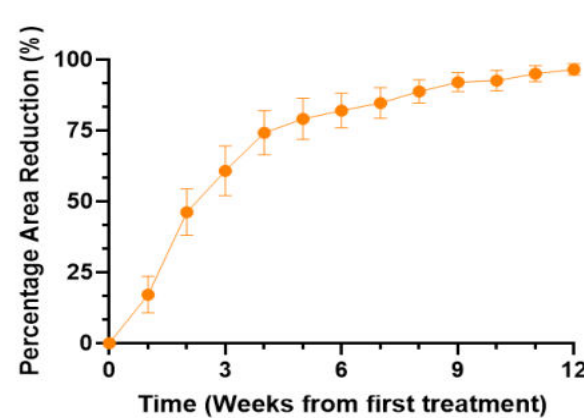


Figure 2. Average percentage wound area (PAR) during the course of the study (n = 10). PAR of total 10 patients was 96% at week 12.

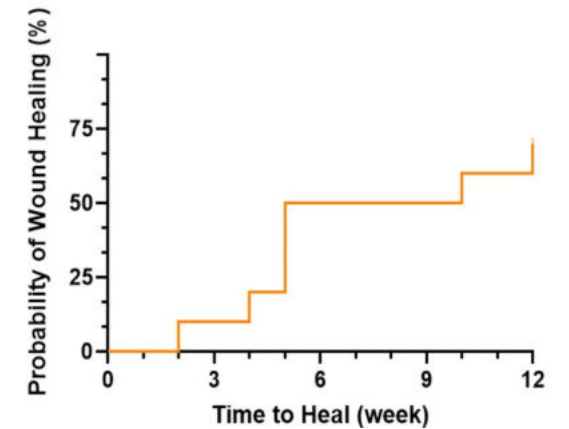


Figure 3. Kaplan-Meier plot of wound healing (n=10).

Experience with Al Qassimi Hospital (EHS) Sharjah - UAE



Experience with Al Qassimi Hospital (EHS) Sharjah - UAE

← **Pre-OP** → ← **Application** → ← **Post-OP** →

Week 1

Week 2

Week 3

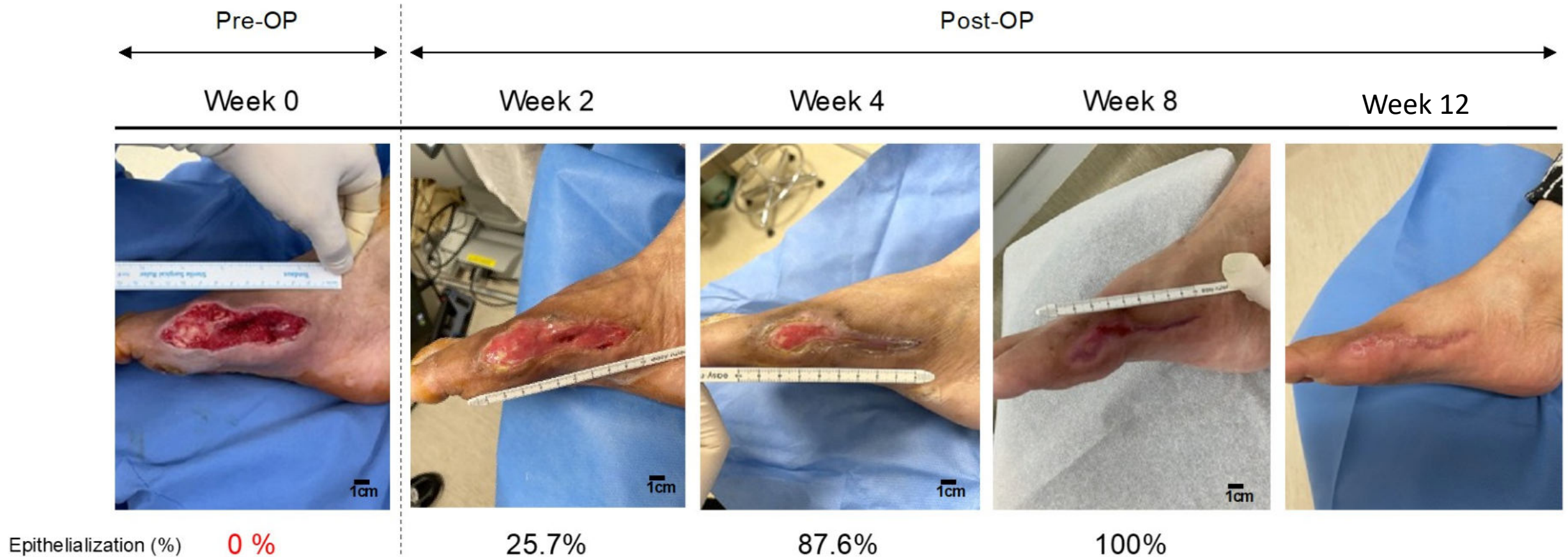
Week 4





Patient a (F/67y, DM Type II)

- ▶ Large, tendon-exposed chronic diabetic foot
- ▶ After 1 treatment, more than 90% regeneration in 4 weeks, full recovery after 8 weeks.



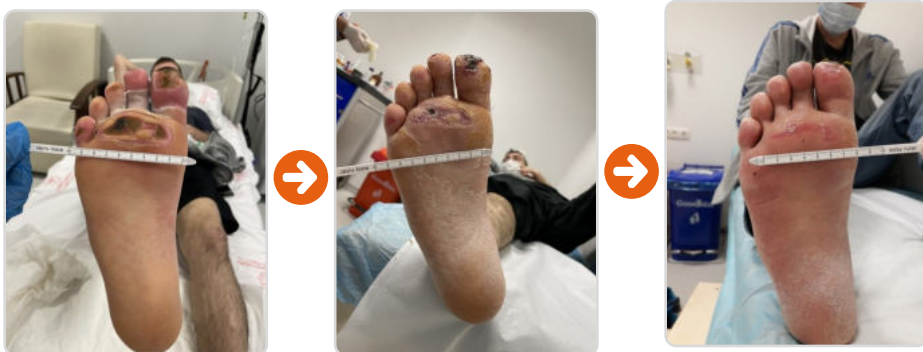
Patient 1 (F/58, DM Type II)

- **Deep ulcer with tendon exposure**
- **100% epithelialization at week 4**



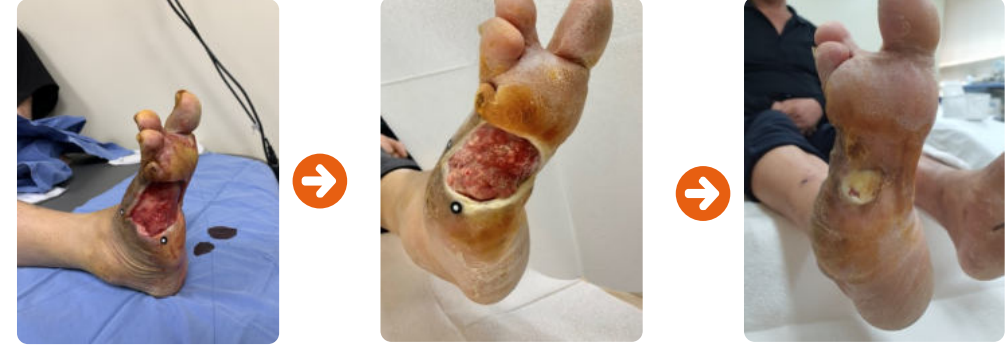
Patient 3 (M/41, DM Type II)

- **Diabetes patient with burn injury on the plantar.**
- **100% epithelialization within 5 weeks without contraction.**



Patient 2 (M/70, DM Type II)

- **Large ulcer across the Rt. foot with 4, 5th toe amputation history**
- **Unsuitable for skin graft poor wound bed condition**

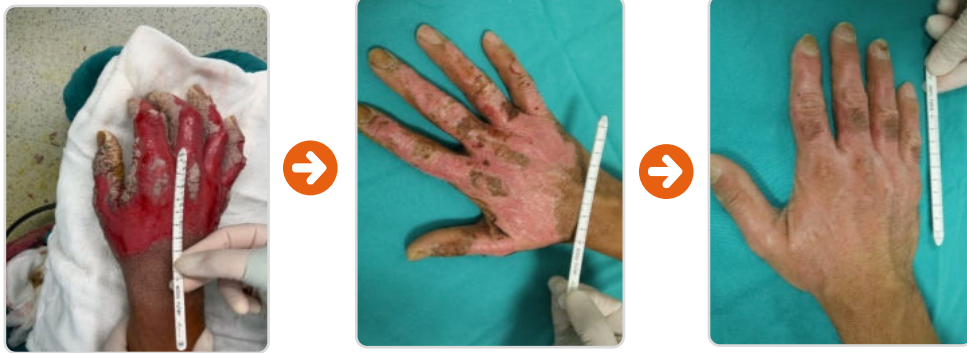


Patient 4 (M/49, DM Type II)



Patient 5 (M/41, 2nd degree burn)

- **100% epithelialization within 1 week after single treatment.**
- **Full restoration of hand function without contraction on the joints.**



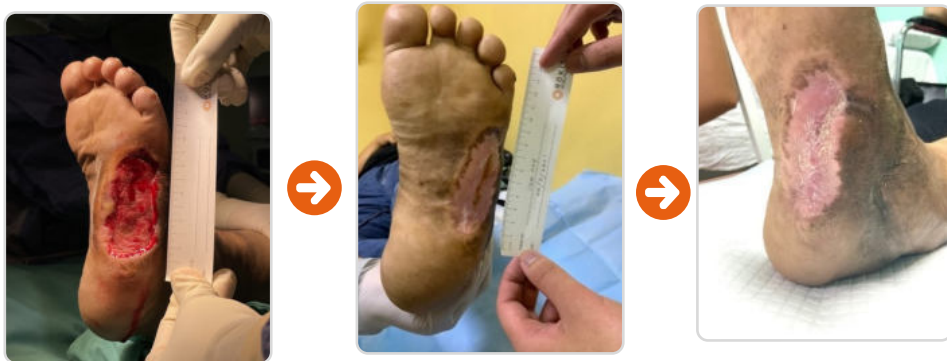
Patient 6 (F/55, DM Type II)

- **Deep ulcer with bone exposure on Rt. Heel.**
- **Accelerated granulation within 2 weeks and healed at week 5.**



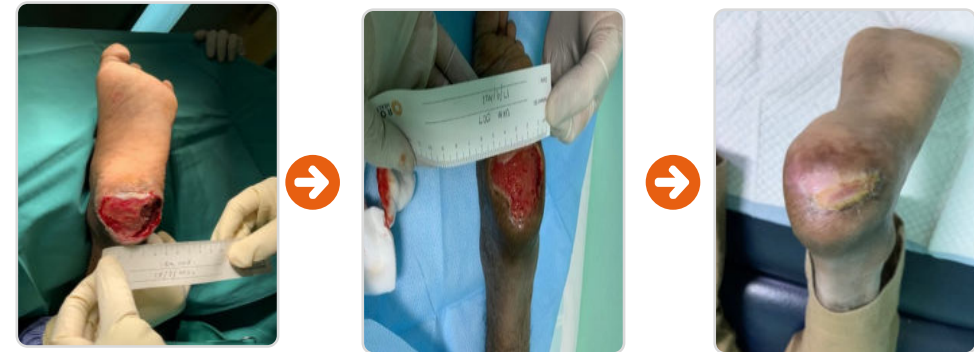
Patient 7 (M/41, DM Type II)

- **Large ulcer on the plantar.**
- **Healed within 10 weeks.**



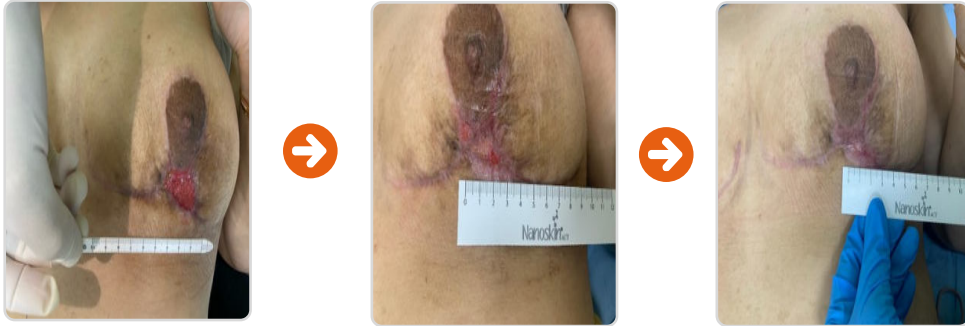
Patient 8 (M/44, DM Type II)

- **Ulcer on Lt. heel where is vulnerable to pressure damage.**
- **Healed within 12 weeks.**



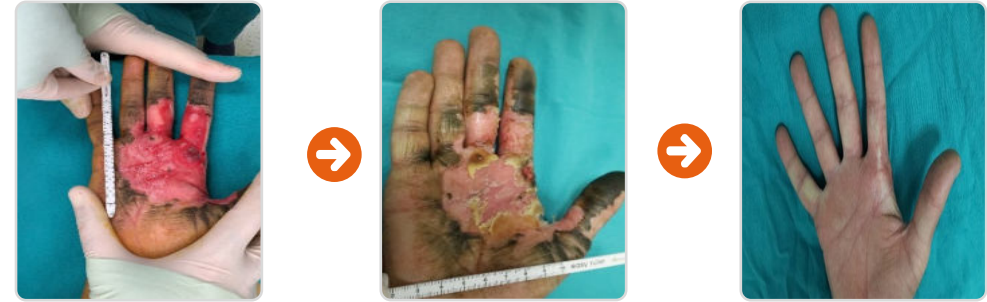
Patient 9 (F/41, complication scar)

- Chronic wounds resulting from complications after breast implant surgery .
- **Recovery within 4 weeks after one treatments**



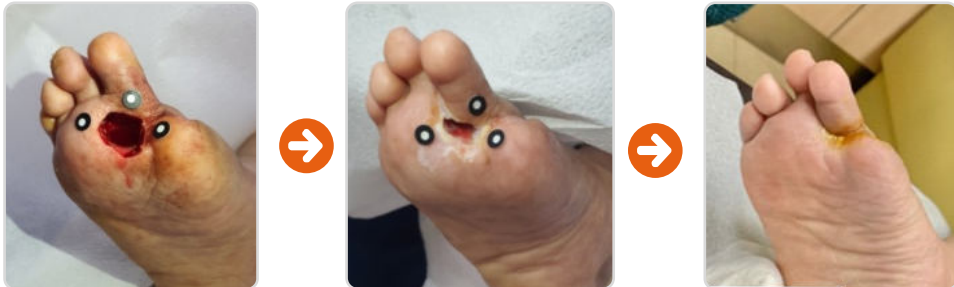
Patient 10 (M/55, 3rd degree of burn)

- 3rd degree of burn.
- **Complete recovery within 2 weeks**



Patient 11 (F/64, DM Type II)

- Toe amputation, chronic DFU patient on dialysis.
- **96% skin regeneration in 4 weeks & Full recovery 12 weeks.**



THANK YOU!

CLINICAL TRIAL IN INDIA; The manuscript has been published to *International Journal of Lower Extremity Wounds (IJLEW)*. (Impact Factor: 2.057)

Management of Diabetic Foot Ulcer with MA-ECM (Minimally Manipulated Autologous Extracellular Matrix) Using 3D Bioprinting Technology – An Innovative Approach

The International Journal of Lower Extremity Wounds
1-8
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Rajesh Kesavan^{1,2}, Changam Sheela Sasikumar^{3,4},
V.B. Narayanamurthy⁵, Arvind Rajagopalan⁶, and Jeehee Kim⁷

Abstract

Chronic foot ulcers are the leading cause of prolonged hospitalization and loss of social participation in people with diabetes. Conventional management of diabetic foot ulcers (DFU) is associated with slow healing, high cost, and recurrent visits to the hospital. Currently, the application of autologous lipotransfer is more popular, as the regenerative and reparative effects of fat are well established. Herein we report the efficacy of minimally manipulated extracellular matrix (MA-ECM) prepared from autologous homologous adipose tissue by using 3D bioprinting in DFU (test group) in comparison to the standard wound care (control group). A total of 40 subjects were screened and randomly divided into test and control groups. In the test group, the customized MA-ECM was printed as a scaffold from the patient autologous fat using a 3D bioprinter device and applied to the wound directly. The control group received standard wound care and weekly follow-up was done for all the patients. We evaluated the efficacy of this novel technology by assessing the reduction in wound size and attainment of epithelialization. The patients in the test group (n = 17) showed complete wound closure with re-epithelialization approximately within a period of 4 weeks. On the other hand, most of the patients in the control group (n = 16) who received standard wound dressings care showed a delay in wound healing in comparison to the test group. This technique can be employed as a personalized therapeutic method to accelerate diabetic wound healing and may provide a promising potential alternative approach to protect against lower foot amputation a most common complication in diabetes.

Keywords

diabetic foot ulcer, autologous fat, lower extremity wound, minimally manipulated autologous extracellular matrix, amputation, 3D bioprinting

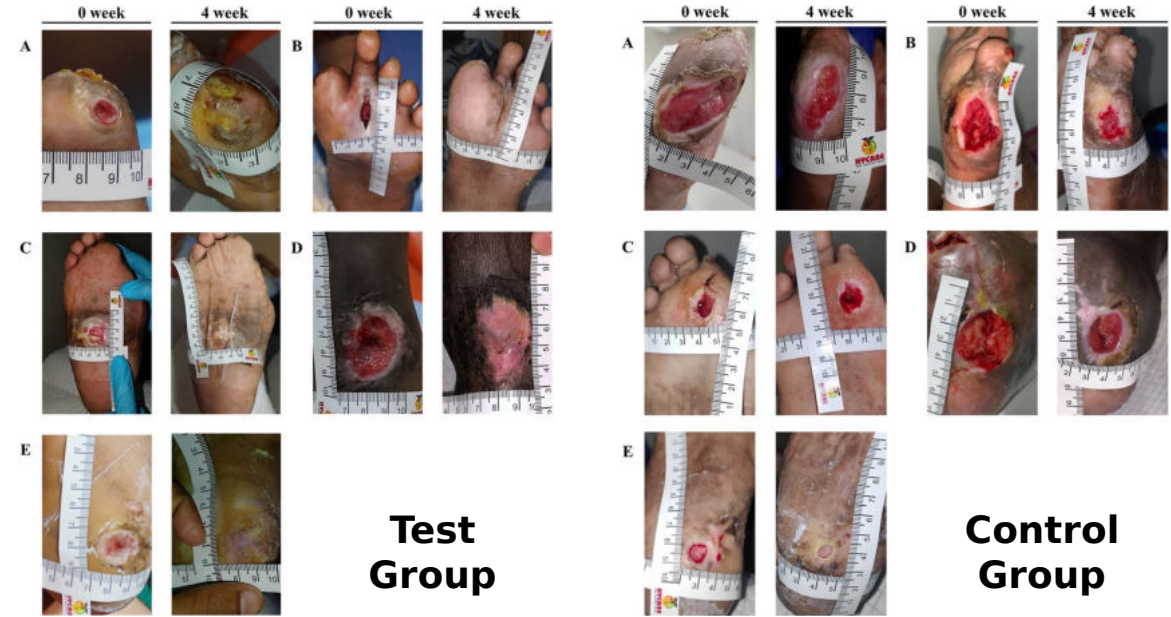


Fig1. Epithelialization and wound healing were completed at 4 weeks after the new treatment in this test/control group. The location of DFU: first toe (A); Plantar fore foot (B); Plantar mid foot (C), Dorsal mid foot (D); Heel (E).

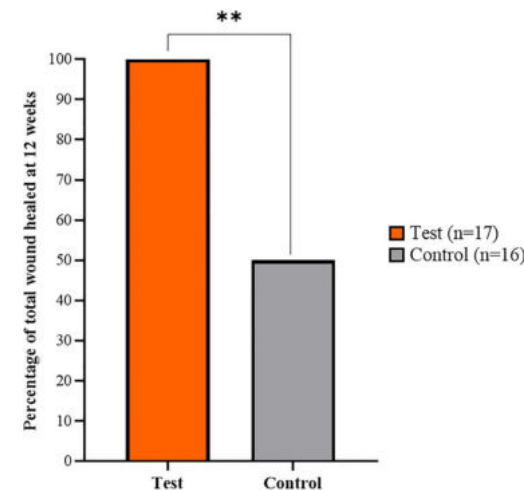


Figure 2. Percentage of subjects presented complete epithelialization at 12 weeks. The bar represents the number of subjects who completed the wound healing process within a period of 12 weeks in percentage. With the help of our innovative treatment in test group, irrespective of wound size and location, we observed all the subjects in the test group were completely healed. In control group, only 50% of the subjects showed healed wound at 12 weeks period. There was statistically significant difference in the test subjects when compared to the control. (P< 0.0001, **).

CLINICAL TRIAL IN INDIA; The manuscript has been published to *Journal of Clinical Medicine (JCM)*. (Impact Factor: 4.96)

An Exploratory, Prospective, Randomized Controlled Trial Comparing a Micronized Adipose Tissue Niche Versus Standard Wound Care to Evaluate Safety and Efficacy in the Management of Diabetic Foot Ulcers

Sik Namgoong MD, PhD | In-Jae Yoon, MD | Seung-Kyu Han, MD, PhD | Ji-Won Son, RN, WCN, | Jeehee Kim, PhD

Background : Numerous studies have demonstrated various properties of micronized adipose tissue (MAT), including angiogenic, anti-inflammatory, and regenerative activities, which can be helpful in wound healing. However, a direct role for MAT in diabetic wound healing has not been demonstrated. The purpose of this exploratory clinical trial was to report the efficacy and safety of a MAT niche for treating diabetic foot ulcers.

Methods : Twenty subjects were randomly divided into MAT niche treatment (n=10) and control groups (n=10). All patients were followed up weekly for 16 weeks. We evaluated the efficacy of the MAT niche treatment by assessing 1) the reduction in wound area after 4 weeks and 2) the percentage of patients who achieved complete wound closure after 16 weeks. All possible adverse events were also recorded.

Results : The wound area was reduced by 4.3 ± 1.0 cm² in the treatment group and by 2.0 ± 1.1 cm² in the control group (p=0.043). The wound reduction rate 4 weeks post-treatment was $77.1 \pm 4.9\%$ in the treatment group and $45.7 \pm 15.6\%$ in the control group (p=0.055). Complete wound healing was achieved after 16 weeks in 8 out of 10 patients (80%) in the treatment group and 3 out of 6 (50%) in the control group (p=0.299). No serious adverse events related to MAT niche treatment were observed.

Conclusion : The early study now suggests that the MAT niche may be an effective and safe method for treating diabetic foot ulcers.

We look forward to larger pivotal studies to confirm these initially promising findings



Figure 1. A diagram showing the flow of patients in the treatment group in this study



Figure 2. A 70-year-old man had a nonhealing diabetic foot ulcer on his right foot for 8 weeks. A micronized adipose tissue niche was applied to the wound for 16 weeks.

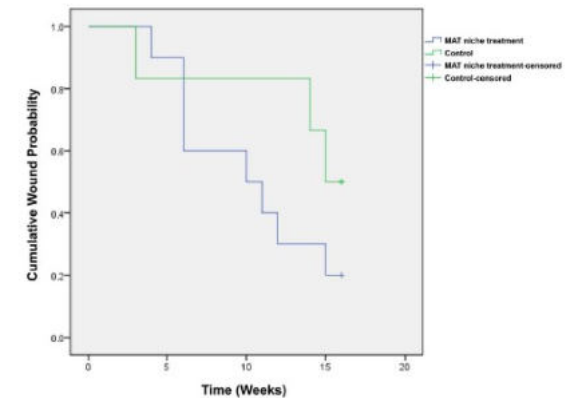


Figure 3. Kaplan-Meier diagram showing results of the time to wound closure. The Kaplan-Meier median times to complete closure were 10.2 ± 1.4 and 13.3 ± 1.9 weeks in the treatment and control groups, respectively (p=0.187, the log rank test of the Kaplan-Meier method).

CLINICAL TRIAL IN INDIA; The manuscript has been published to *Plastic and Reconstructive Surgery (PRS Global Open)* (Impact Score: 1.60)

A pilot study using graft of autologous minimally manipulated homologous adipose tissue (AMHAT) for treatment of non-healing diabetic foot ulcers

David G. Armstrong | Zachary Rasor, DPM | Steven G. Harris | Charles M. Zelen | Jeehee Kim | Adam L. Isaac

ABSTRACT

Background: Diabetic foot complications are increasingly common, complex, and costly, and the need to develop effective treatments for chronic diabetic foot ulcers (DFU) is critical. Methods: A single-arm pilot study of ten consecutive patients with a history of a chronic DFU, treated with autologous minimally manipulated homologous adipose tissue (AMHAT), dispensed by a specialized bioprinter device, was performed. Patients with non-healing DFUs present for more than 4 weeks, and refractory to standard of care therapies were included. Wounds were treated with a single application of AMHAT, and then followed weekly for up to 12 weeks, or until the wounds healed. The primary outcome measure was complete epithelialization of the wound up to 12 weeks after the treatment. Secondary outcome measures included wound size and/or volume reduction, assessment of Wagner grade, and time to closure.

Results: Complete closure was achieved in 60% of wounds. Five wounds were healed by 6 weeks, and one at 8 weeks. The mean PAR at 12 weeks was 78.3% (SD: 33.23). The mean time to closure in these wounds was 49.1 days (95%CI: 29.9-68.3). No adverse events were reported.

Conclusions: **Single treatment of AMHAT is a safe and effective treatment modality for chronic DFUs using the patient's own adipose tissue.**

Further studies are warranted to explore the full potential of 4D bioprinting for wound healing in this high-risk population.

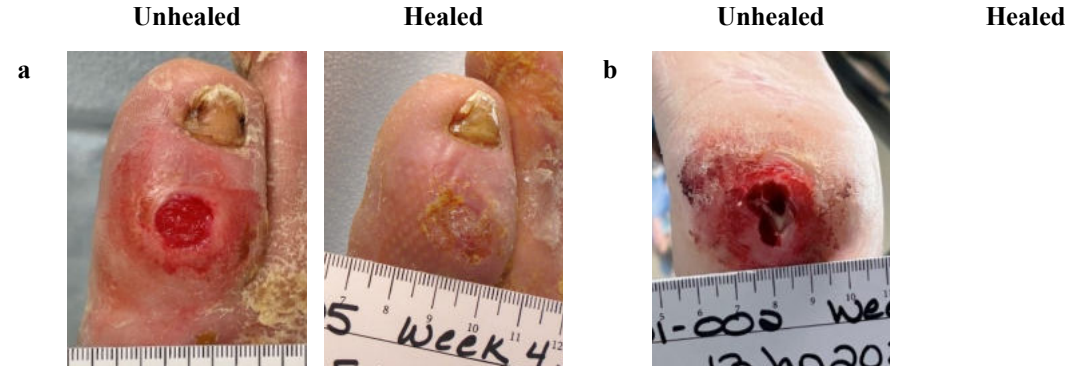


Figure 1. Comparison before and after improvement of the wound area after AMHAT application. a) patient at 4 weeks later and b) patient at 5 weeks later healed.

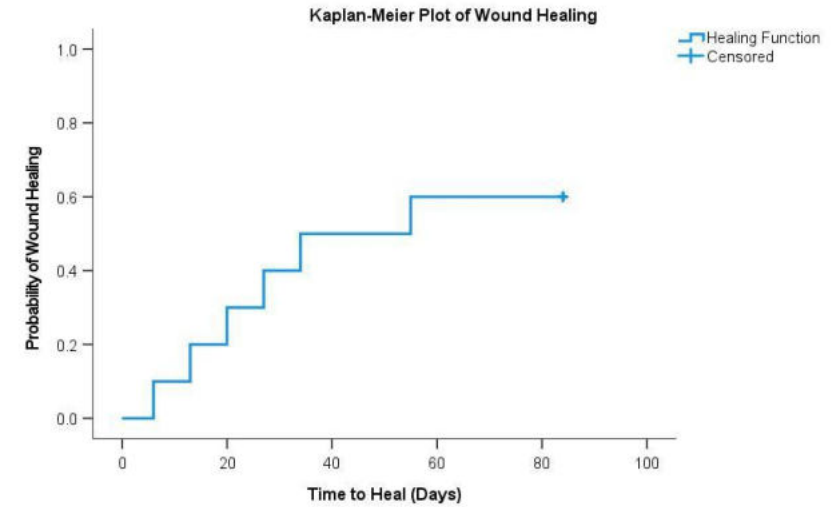


Figure 2. Time to heal (days) by Kaplan-Meier Plot of Wound Healing. The mean time to closure in these wounds was 49.1 days (95%CI: 29.9-68.3). The Kaplan-Meier plot of wound healing

CLINICAL TRIAL IN INDIA; The manuscript has been published to *Wounds* (Impact Factor: 1.09)

Graft of 3D bio-printed autologous minimally manipulated homologous adipose tissue for the treatment of diabetic foot ulcer

Ahmet Çınar Yaştı | ALI Emre AKGUN | Aziz Ahmet Sural | Jeehee Kim | Merve Akan

Abstract

Introduction

Adipose-derived stem cells are multipotent precursor cells which have the ability to differentiate into cell lineages associated with the regeneration of tissues, such as fibroblasts, keratinocytes, and endothelial cells. We investigated the efficacy of autologous minimally manipulated homologous adipose tissue (AMHAT) with 3D bioprinting technology in diabetic foot ulcer (DFU).

Material and Methods

Twenty patients were enrolled in our clinical prospective observational study. The primary endpoint was a reduction in the size of DFU, and the secondary endpoints were the epithelialization rate and amount of granulation of wound bed at weekly assessments. The Dr. INVIVO 3D bioprinter (ROKIT Healthcare, Inc) was used to produce AMHAT in the customized shape of DFU. The data was obtained using photography and computerized digital surface calculation.

Results

The mean wound size at the time of hospitalization was 7.529 cm². All but one of the wounds were completely epithelialized at the ninth week. The mean wound areas decreased at weekly assessments for the first seven weeks of treatment compared to the pre-application ($p=0.000$, $p=0.000$, $p=0.001$, $p=0.002$, $p=0.014$, $p=0.015$, and $p=0.014$, respectively). When the mean decrease in the wound size was compared between each consecutive week, there were decreases at each of the first seven weeks ($p=0.000$, $p=0.002$, $p=0.004$, $p=0.014$, $p=0.016$, $p=0.045$, and $p=0.038$, respectively). The mean time to the complete closure was 32.20 ± 23.862 days.

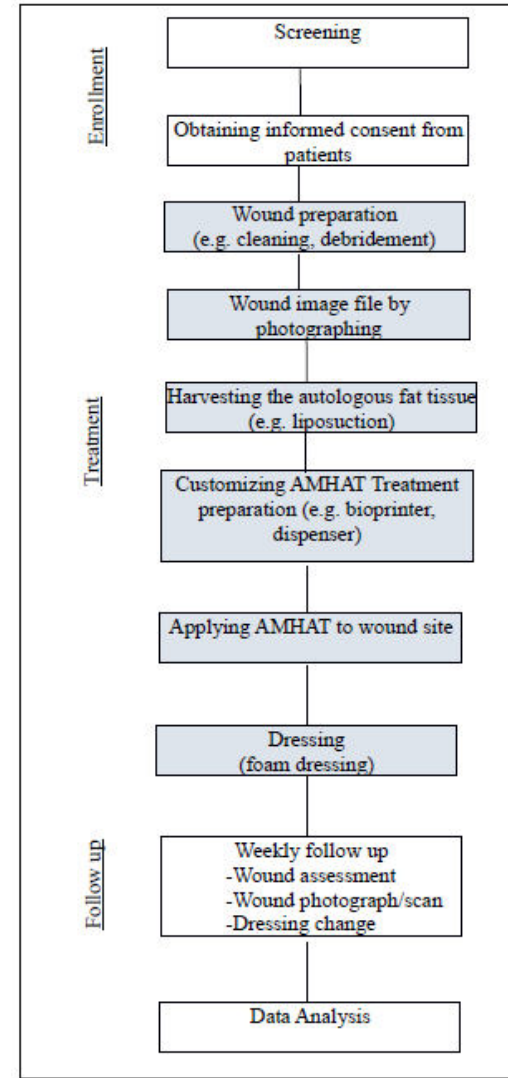


Figure 1. Study design



Figure 2. Before AMHAT



Figure 3. After AMHAT