Revolutionizing Wound Care: Precision Healing with Personalized Adipose Tissue Grafts Generated Using an FDA-Cleared 3D Printing System

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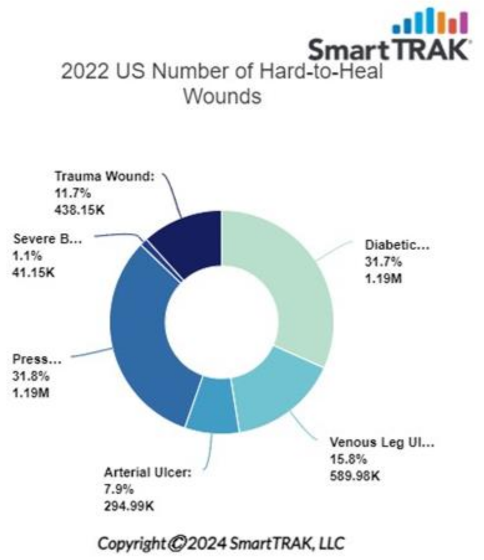
Introduction

The burden of diabetes in the U.S. has reached staggering proportions, with 11.4% of the population, or 38.4 million, adults affected as of 2021 *(ADA data)*. Among the myriad of complications of diabetes, diabetic foot ulcers (DFUs), and venous ulcers stand as significant challenges, with a lifetime risk of 34% and an annual incidence ranging from 1.6 to 2.1 million cases *(SmartTrak data)*.

Alarmingly, over half of these ulcers become infected, often necessitating hospitalization and, in severe cases, lower limb amputation. Consequently, there is an urgency to develop innovative therapies to bolster wound healing in individuals predisposed to diabetic foot complications.

Current advanced wound care solutions, such as skin substitutes, oxygen therapies, and negative pressure therapies, have significantly progressed the field. However, these technologies lack personalization to individual patients, tailoring for specific wounds, utilization of patients' stem cells for chronic wound healing, and often require multiple applications.

This study presents the first commercial application of a 3D-printed adipose tissue matrix graft, personalized and customized for patients with chronic wounds, using the Aplicor 3D system in the United States. The method employs an FDA-cleared 3D adipose tissue printer, which creates a patient-wound-specific graft that requires a single graft application during treatment (8–12 week period).



Case Study

60-65-year-old male patient diagnosed with type-2 diabetes mellitus (DM2) greater than 8 years ago presented at the clinic with a non-healing ulcer on his shin. This diagnosis was initially accompanied by sensitive and motor peripheral neuropathy, metatarsophalangeal arthropathy with no signs of osteomyelitis and diabetic arthropathy. Patient also presented with a lung Carcinoma.

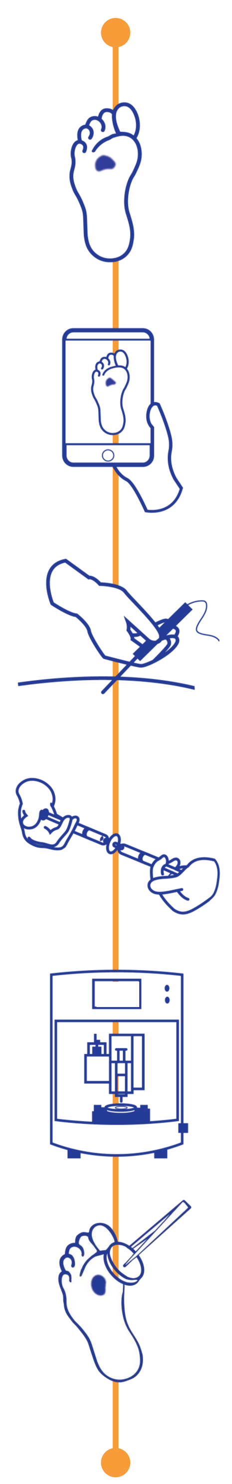
As per the patient, the ulcer had persisted for 6-8 months. The ulcer never completely healed during that period, and he needed several admissions in hospital due to recurrent infections. On one occasion, he needed debridement and IV antibiotics as well. Currently, and according to the patient himself, although he is aware of the main considerations in managing diabetic feet and venous ulcers, his compliance has not been as constant as it should have been, especially regarding diet, smoking, and exercise. He has an appropriate metabolic control of his disease with 7.4% glycated hemoglobin values. The approximate size of the wound after debridement was 56 cm^2.

PROCEDURE

Two weeks prior to the use of the APLICOR system, the patient's blood flow in the right limb was evaluated. The angiogram revealed a significant occlusion in the anterior tibial artery (See Fig A). The patient's hemodynamics was successfully improved using a balloon angioplasty procedure. Blood flow improvement was maintained the week prior and of the APLICOR treatment.

The following procedure was used to create and apply the APLICOR 3D patch. The procedure involved a surgical debridement of the wound with a 15-gauge scalpel, followed by the generation of a stereolithography (stl) file for 3D printing. To create the stl file, an image of the debrided wound bed was taken using the AiD regen tablet and software. The system automatically generated and transferred the file to the 3D printer and created a raised outline of the wound bed for the creation of the adipose matrix graft. While the outline of the wound bed was being printed, liposuction was performed on the patient using a manual syringe set up and tumescent solution. Approximately 20-35mls of liposuction aspirate was harvested from the patient. The harvested fat underwent a series of micronizations that serially reduced the size and improved the flowability of the adipose matrix. The micronized fat was washed with saline and loaded on the printer with a 5ml BD syringe and a one inch 21-gauge needle. An adipose matrix graft was generated using the thrombin fibrin protocol on the printer to create a gel like structure with the same shape as the wound bed. Once printing was completed, the adipose tissue graft was gently placed over the debrided ulcer. The graft was oriented with the top surface facing the debrided wound and aligned to maximize the edge contact between the wound bed and graft. The graft was covered with a nonadherent dressing, gauze, and Curlex.

In the weeks following treatment, the patient underwent regular monitoring and care. Each visit included a comprehensive assessment, encompassing vital signs, evaluation of adverse events, and the review of concomitant medications. Additionally, gentle debridement was conducted if necessary, and wound progress was meticulously documented through digital photography and measurement post debridement.



Results

- Angioplasty successfully improved blood flow in the anterior right tibial artery
- APLICOR 3D System was able to generate a 3D adipose graft that matched the exact shape of the debrided wound bed in the OR (56 cm^2), by the patient's bedside
- End-to-end, the procedure lasted approximately 75 minutes
- Greater than 50% wound closure was noted at 4 weeks
- Complete closure with re-epithelialization of the chronic wound was noted at 8 weeks
- A single application of the graft was required for complete closure of the wound over a period of 8 weeks

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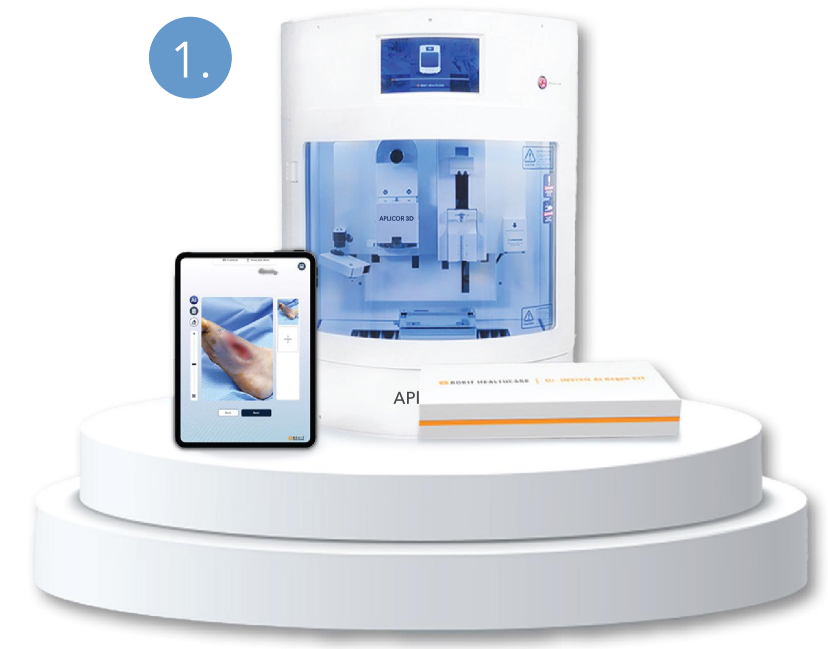

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Figure 1: APLICOR 3D print procedure involves surgical debridement of the wound, followed by the generation of a 3D printed wound bed using AiD regen tablet and software. Liposuction fat is then micronized, washed, and loaded onto the printer to create a gel consistency adipose matrix graft. The graft is oriented for optimal edge contact and placed over the debrided ulcer and covered with non-adherent dressing.

Figure 2 (A-Q Left):
A and C: Pre angioplasty angiogram.
Figure B and D: Post Angioplasty angiogram.
Figure E vascular ulcer on patient prior to angioplasty.
Figure F and G pre debridement on day of Aplicor 3d application.
Figure H, I, and J: APLICOR 3D graft application.
Figure K and L: Week 1 after graft application. Figure M: Week 2 after application.
Figure N: Week 3 after application.
Figure O: Week 4 after application.
Figure P: Week 6 after application.
Figure Q: Week 8 after application.

Discussion

There are several approaches to treat DFUs and VLUs in diabetic patients. However, the currently employed methods rely on multiple applications and are often not tailored to the patient's wound or biology. APLICOR 3D presents a revolutionary approach to print 3D adipose matrix grafts that are both safe and efficacious. What is more, only a single application of the graft is required over a 12-week treatment course. This technique involves the transfer of adipose tissue rich in growth factors, such as insulin-like growth factor, hepatocyte growth factor, transforming growth factor-β 1, and vascular endothelial growth factor. These bioactive molecules play pivotal roles in fostering angiogenesis, epithelialization, and wound remodeling. Moreover, adipose stem cells and the anti-inflammatory cytokines, proangiogenic factors, and healing-related peptides present in autologous fat may further exert favorable effects on wound healing processes.

Tailoring the wound graft to the exact size of the wound bed ensures maximum surface and edge-to-edge contact, allowing for rapid cell infiltration of cells into and granulation of the wound bed. Granulation tissue, a highly vascularized network comprising fibroblasts and macrophages embedded in a collagen and fibrin matrix, plays a critical role in wound healing. It offers initial strength, promotes blood circulation, facilitates migration of epithelial cells and fibroblasts, and helps fend off infections.

Harnessing the potential of advanced technologies, APLICOR 3D (ROKIT Healthcare, Seoul, South Korea and Tides Medical, Lafayette, LA) offers a tailored wound healing solution built on a 3D bioprinting platform for tissue regeneration. This novel approach holds promise for revolutionizing the management of chronic ulcers, offering renewed hope for patients grappling with this debilitating complication of diabetes. Building on the success seen in this study, along with larger future studies, the 3D bioprinter may become an important tool in the patient's pursuit of ulcer-free, activity-rich days.

Conclusions

- APLICOR 3D introduces a revolutionary approach to treat DFUs and VLUs with 3D adipose matrix grafts.
- Single application of adipose matrix graft, generated by the APLICOR 3D system potentially offers safe and efficacious treatment for chronic wounds.
- Adipose matrix grafts foster angiogenesis, epithelialization, and wound remodeling.
- AiD regen software provides tailored wound grafting, enhancing edge contact, promoting rapid cell infiltration and granulation tissue formation.
- APLICOR 3D's advanced technology holds promise for revolutionizing chronic ulcer management, offering hope for patients with diabetes. Further studies could solidify the role of 3D bioprinters in achieving ulcer-free, activity-rich days for patients.

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