
بسم الله الرحمن الرحيم

Diabetic Foot Prevention and Management

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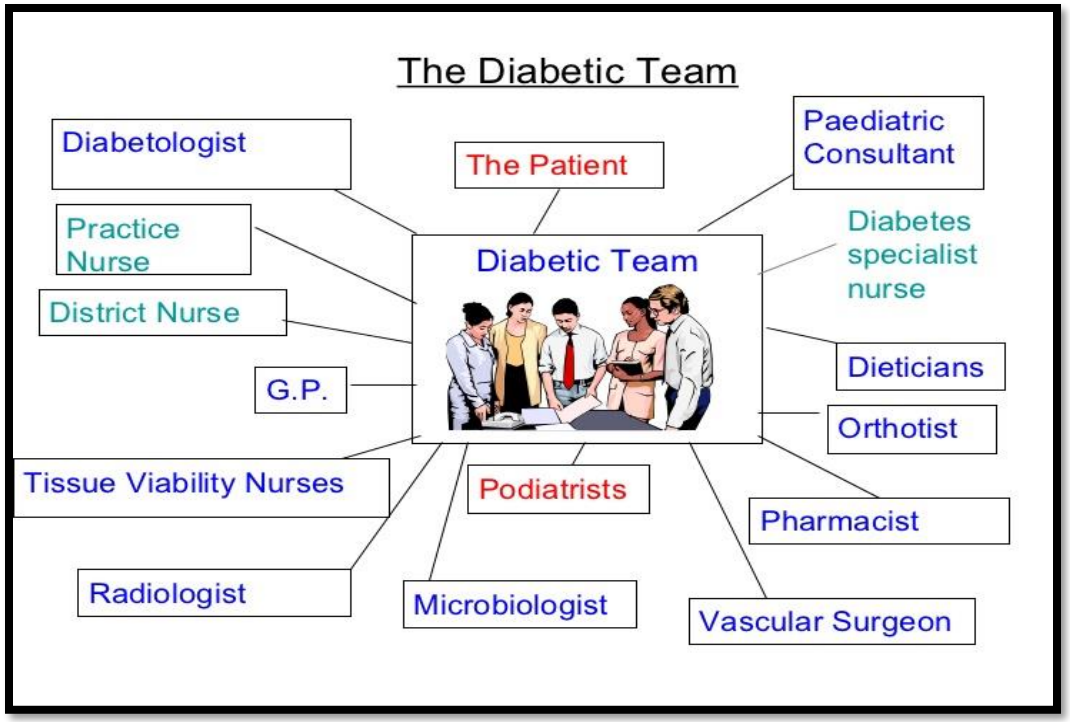
Professor of Endocrinology &Metabolism
EMRI-TUMS
2021

Diabetic Foot Management

Multidisciplinary DF Management

- Multidisciplinary foot care team
- Foot protection team



Wound Assessment

DFU Principle of Treatment

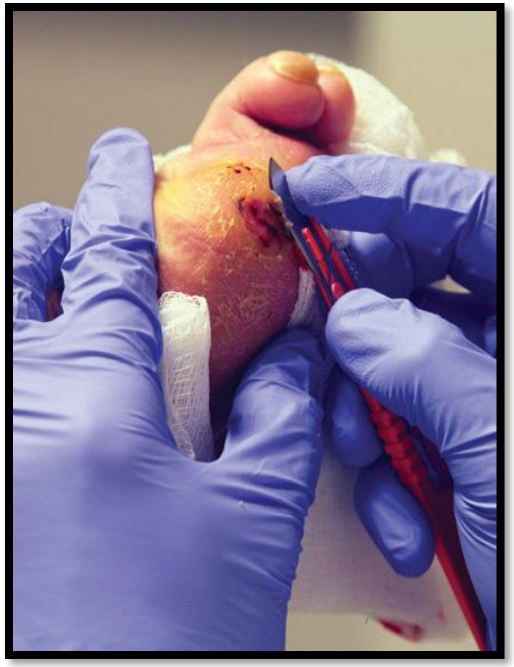
- **Debridement**
- **Exudate managing & Dressing**
- **Control of Infection**
- **Offloading**
- **Revascularization**

Debridement

Definition: Debridement is the process of removing nonliving tissue from pressure ulcers, **burns**, and other **wounds**.

Types:

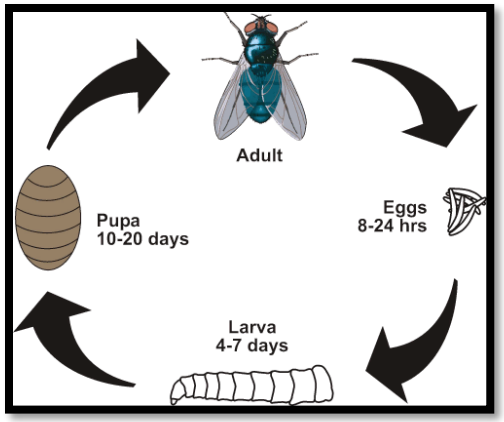
- **Autolytic**
- **Mechnical**
- **Biological**
- **Ultrasonic**
- **Hydrosurgical**
- **Sharp**
- **Surgical**



Principal of Debridement: The Diabetic Foot, June 2004

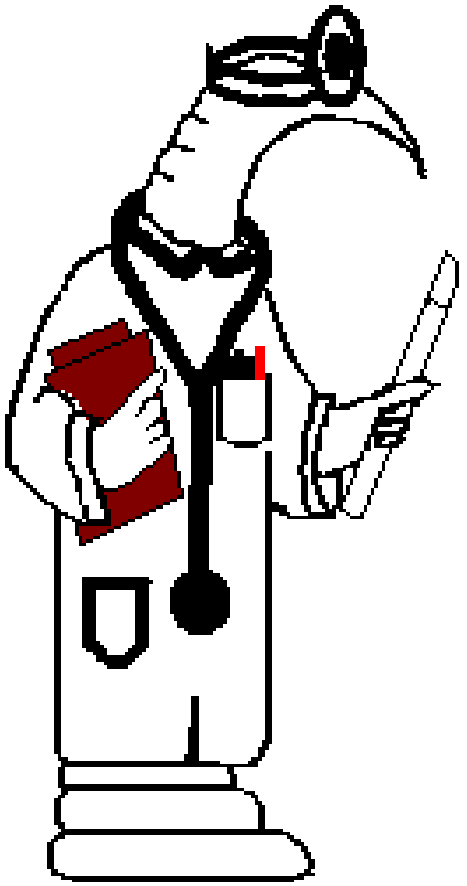
Maggots (larva-therapy)

- The larvae of the green bottle fly (Luciliasericata) used to debride ulcers, especially in the neuro-ischaemic foot.
- Sterile maggots obtained from a medical maggot farm.
- Larvae produce secretions with antimicrobial activity against Gram-positive cocci, including Methicillin-Resistant Staphylococcus Aureus (MRSA).



Maggot Therapy

- Diversity of wound types
- Remove necrotic flesh
- Antimicrobial properties (MRSA)
- Promote Wound Healing



Soring

ORIGINAL RESEARCH

Low-Frequency Ultrasound Debridement in Patients with Diabetic Foot Ulcers and Osteomyelitis

Sareh Amini, MD[1]; Abolfazl ShojaeeFard, MD[2]; Zohreh Annabestani, MD[1]; Mohsen Rezaie Hammami, MD[1]; Zahra Shalganmehr, BS[1]; Bagher Larijani, MD[1]; Shahrzad Mohseni, MD[1]; Hamid Reza Afshani, MD[3]; Maryam Aboee Rad, BS[1]; Mohammad Reza Mohajeri-Tehrani, MD[1]

WOUNDS 2013;25(7):193-198

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Abstract: *Background.* Although debridement plays a significant role in the healing of diabetic foot ulcers, it may delay the healing process by damaging the granulation tissue. In this study, the efficacy of low-frequency ultrasound (LFU) in chronic wound healing in diabetic foot ulcers in patients with osteomyelitis was evaluated. *Methods.* This randomized clinical trial was conducted on 40 patients with diabetes recruited from the Diabetic Foot Ulcer Clinic of the Endocrinology and Metabolism Research Center of Tehran University of Medical Sciences, Tehran, Iran. All patients with a grade 3 ulcer (Wagner Classification) with 0.6 ≤ ankle brachial index ≤ 1.2, were included. Patients were divided into 2 groups; 1 group received ultrasound-assisted wound therapy (UAW) in conjunction with standard wound care (n = 20) and the control group received only standard wound care. Patients were followed for 6 months. *Re-*

Sonography assisted Debridement

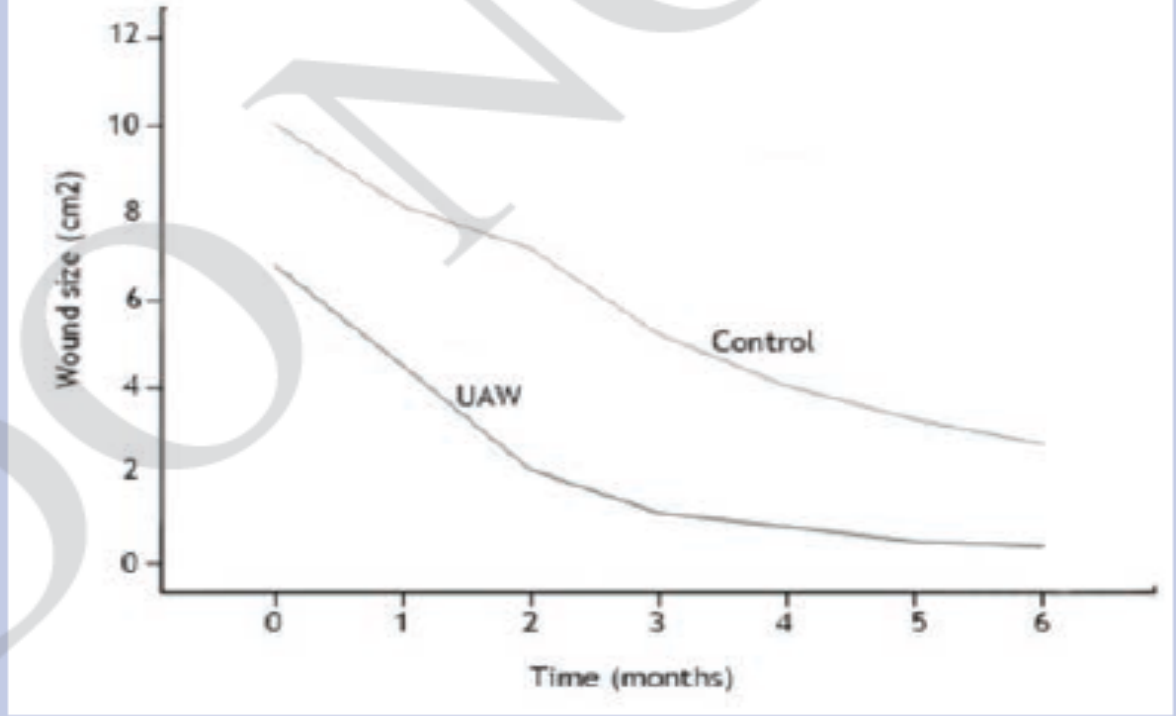
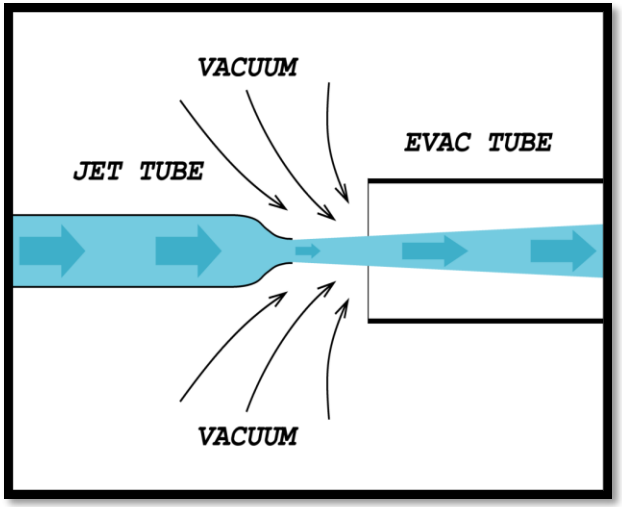


Figure 2. Visual representation of wound size reduction percentages between the 2 study groups, according to time and the initial size of ulcers.

Wound 2013,25(7) 193-198

Hydro-surgery VersaJet

- To debride wounds using a high velocity stream of sterile saline.
- The Venturi effect creates a localized vacuum across the operating window, which simultaneously holds, cuts and removes tissue, while aspirating debris from the operating site.



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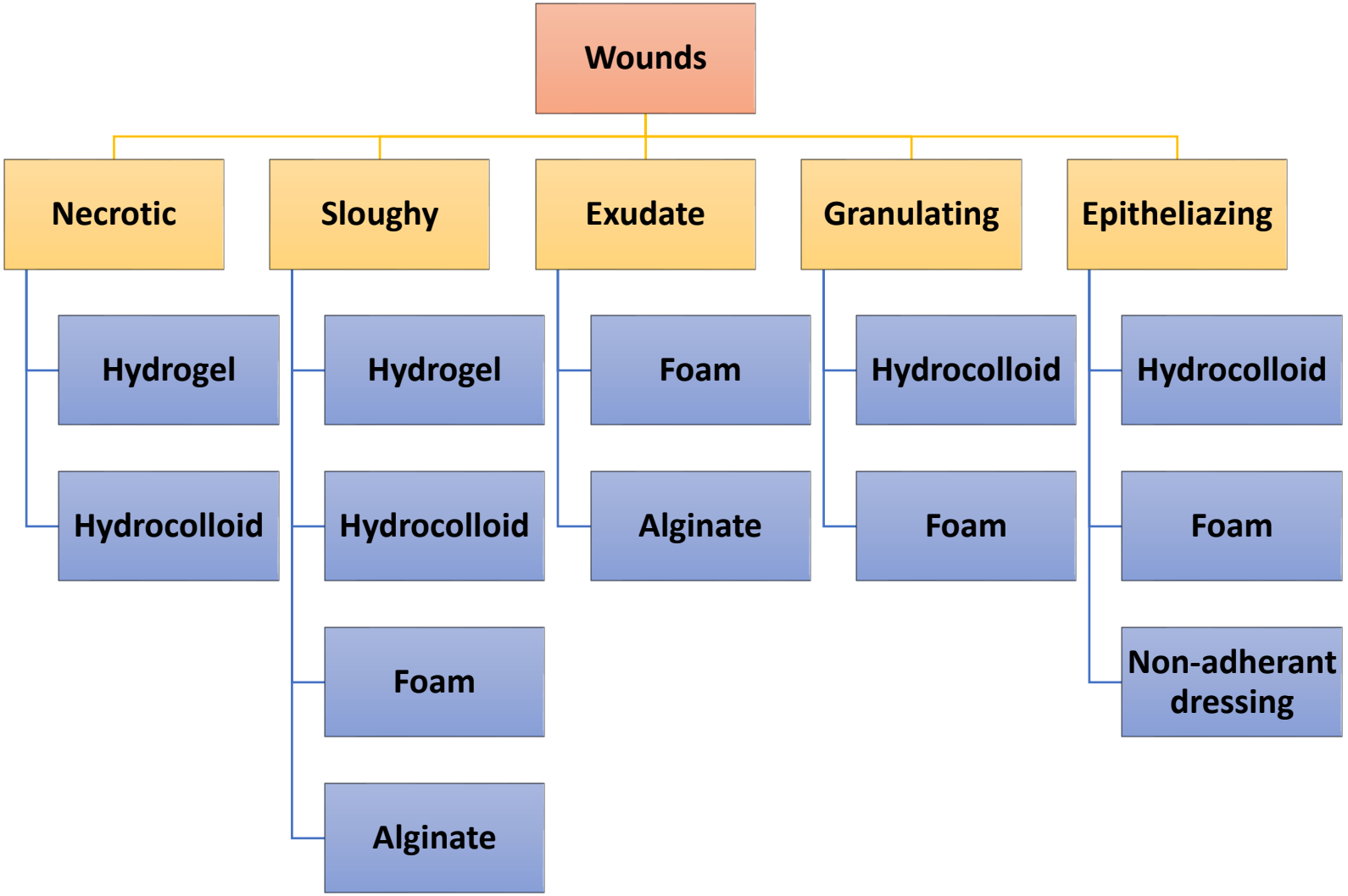
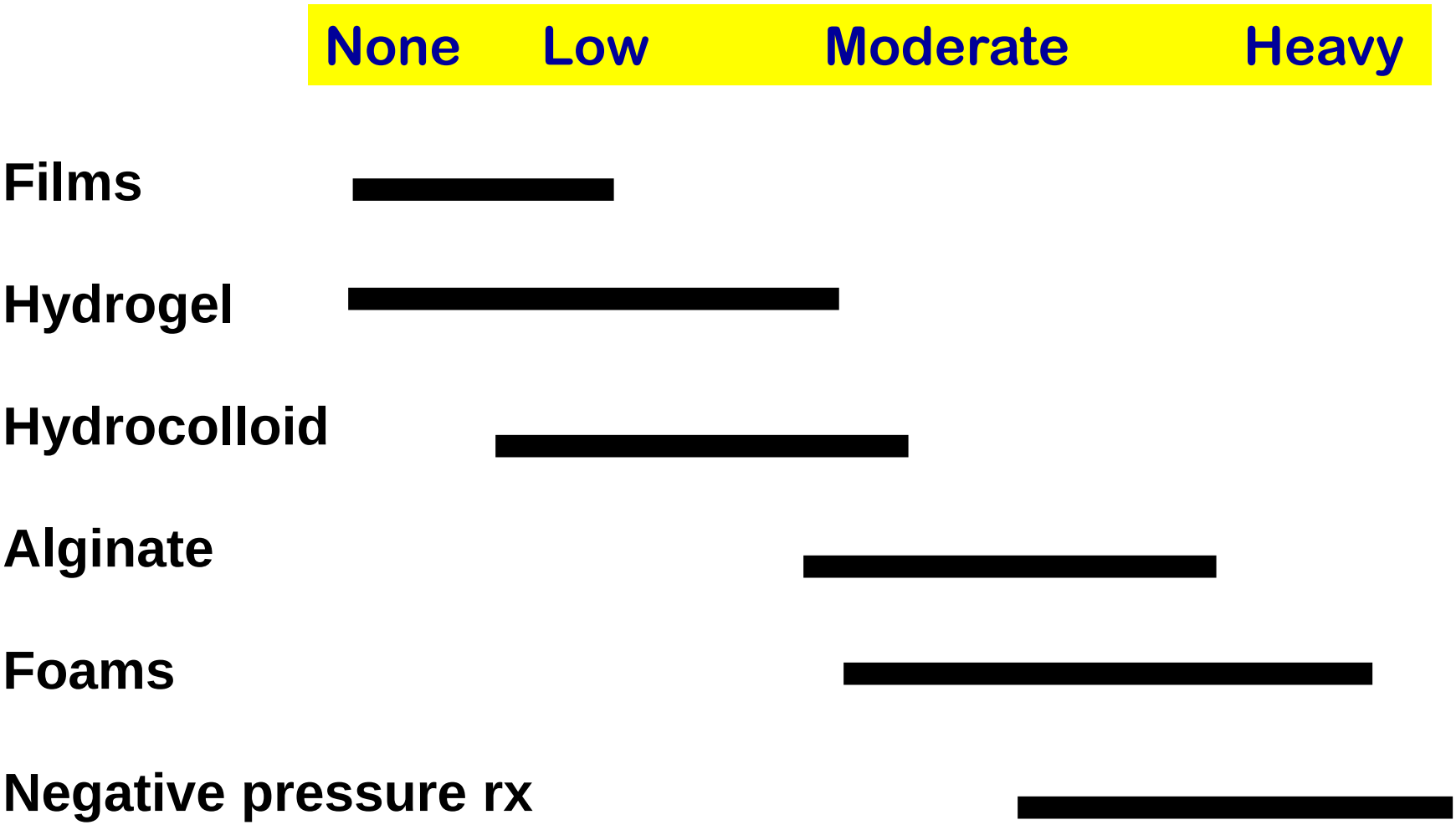
Dressing


Wounds
Necrotic
Sloughy
Exudate
Granulating
Epitheliazing
Hydrogel
Hydrocolloid
Hydrogel
Hydrocolloid
Foam
Alginate
Foam
Alginate
Hydrocolloid
Foam
Hydrocolloid
Foam
Non-adherant dressing

Managing Moisture Imbalance



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Antibiotic

Microbial Evaluation: Principals of Wound Culture

Microbial Evaluation

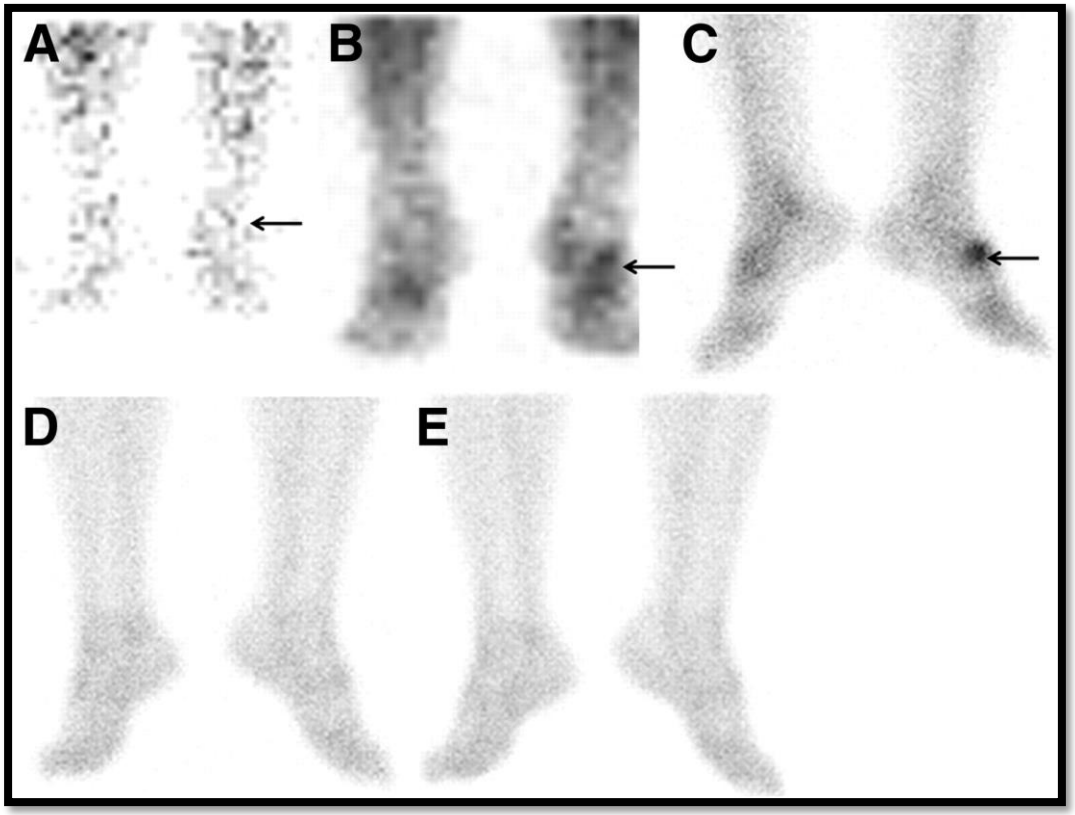
Plain radiograph of the right foot of last patient Osteomyelitis of the fifth metatarsal head and the proximal phalanx of the fifth toe, subluxation of the metatarsophalangeal joint, calcificationof the digital artery between the first two metatarsals and osteoarthritis of the first distal phalangophalangeal joint of the hallux .

Microbial Evaluation...

Diabetic Foot MRI

Microbial Evaluation...

Three phasic Scan



Infection – deep compartment

- Grossly visible bone or ability to probe to bone
- Ulcer size larger than 2 cm^2
- Ulcer duration longer than one to two weeks
- Erythrocyte sedimentation rate (ESR) >70 mm/h

Infection – deep compartment…

Oral agents for empiric treatment of mild to moderate diabetic foot infections

SINGLE-drug regimens with activity against streptococci and staphylococci (MSSA)
Cephalexin **or**
Dicloxacillin **or**
Amoxicillin-clavulanate **or** clindamycin
TWO-drug regimens with activity against streptococci and MRSA
Clindamycin* **or**
Linezolid **or**
Penicillin **or** cephalexin **or** dicloxacillin **PLUS** Trimethoprim-sulfamethoxazole **or** doxycycline

Infection – deep compartment…

TWO-drug regimens with activity against streptococci, MRSA, aerobic gram-negative bacilli and anaerobes
Trimethoprim-sulfamethoxazole
PLUS
Amoxicillin-clavulanate
-OR-
Clindamycin
PLUS
Ciprofloxacin **or** levofloxacin **or** moxifloxacin

DFU Principle of Treatment

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- **Offloading**
- **Revascularization**

Offloading Devices

- Casts
- Temporary shoes
- Felt padding
- Crutches
- Knee scooters
- Wheelchairs
- Zimmer frames
- Electric carts and buggies
- Insoles

Total contact cast

- Efficient method to decreases forefoot plantar pressure by keeping the ankle at 90 degrees
- Can not be used in infected wounds!!

Removable cast walker

- Decreases forefoot plantar pressure by keeping the ankle at 90 degrees
- Can be used in infected wounds!!
- Acceptability is higher than TCC

Half shoes

Dissipates ground-reactive forces on the forefoot and heel by eliminating propulsive gait.

Felt Padding

- Semi-compressed adhesive felt padding
- To divert pressures from ulcers

Knee Scooters

- An alternative to crutches
- Placing the weight of the body on the scooter's knee pad

Wheelchairs

A lightweight folding wheelchair can be of great help in achieving maximal off-loading

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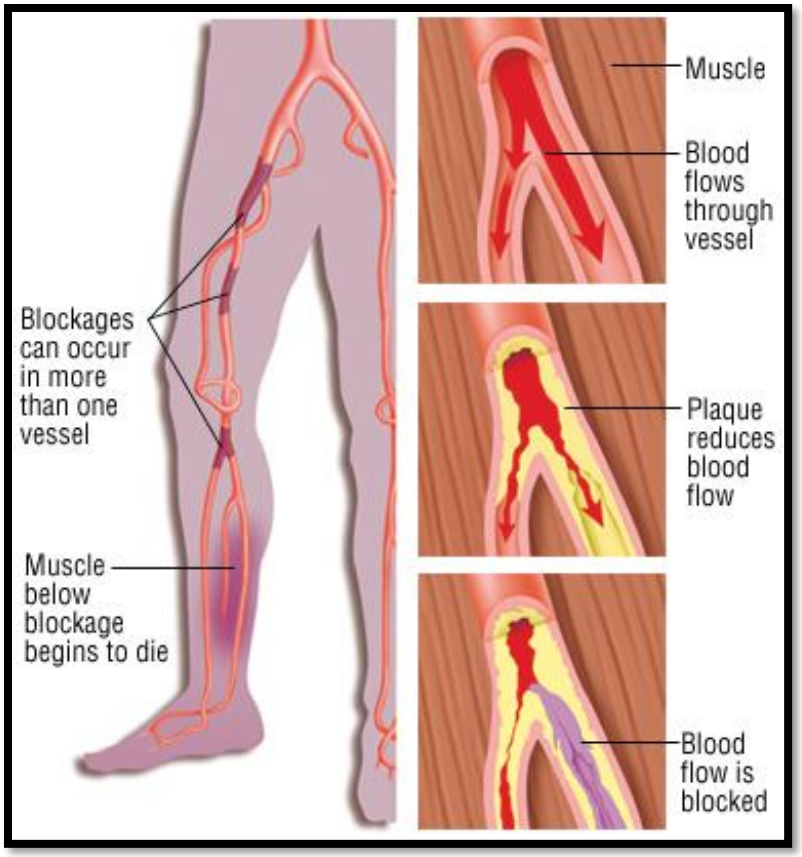
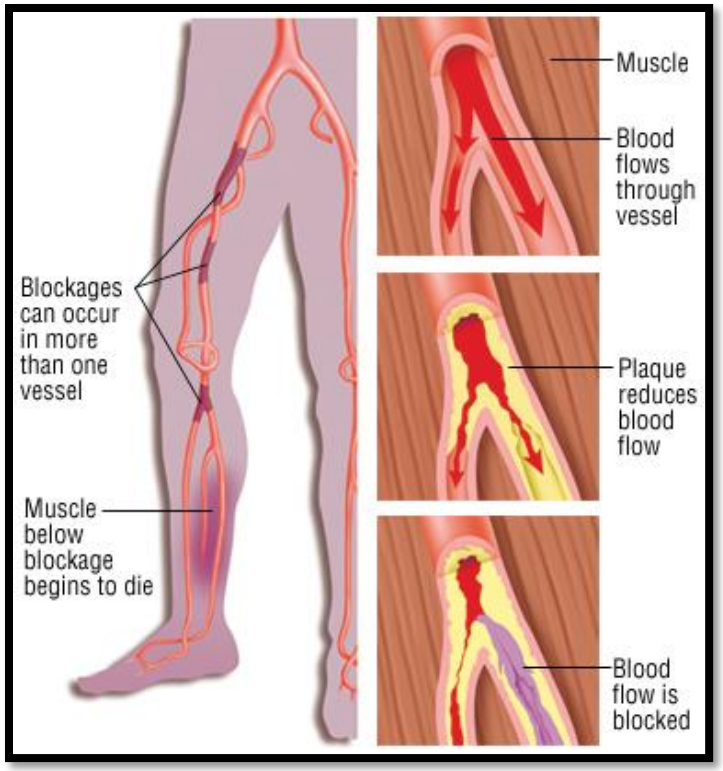
Revascularization



Revascularization

Studies reported herein appear to demonstrate improved rates of limb salvage associated with revascularization compared with the results of non-revascularized patients with diabetes, PAD and ulceration



Novel Treatments of Diabetic Foot

Novel Treatments

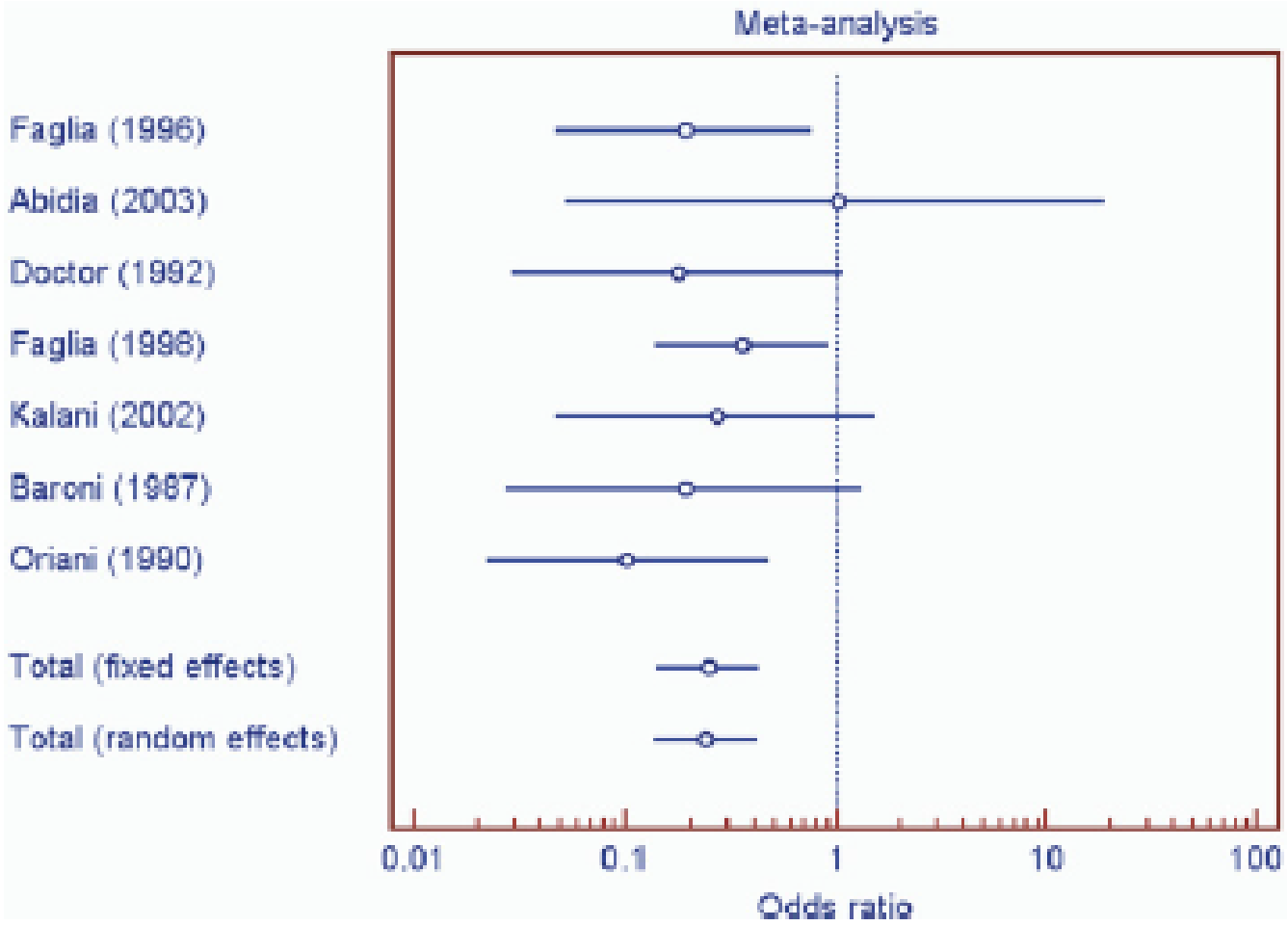
- **Hyperbaric Oxygen**
- **Ozone Therapy**
- **NPWT (Vacuum Therapy)**
- **Laser Therapy**
- **Shockwave Therapy**
- **Cold Plasma**
- **Skin Graft**
- **Bioimplant**
- **Plasma Rich Platelet (PRP)**
- **Stem Cell Therapy**
- **Herbal Therapy**

Hyperbaric oxygen

- Hyperbaric oxygen accelerates the healing of ischaemic DFU.
- Reduce the number of major amputations in ischaemic diabetic feet.

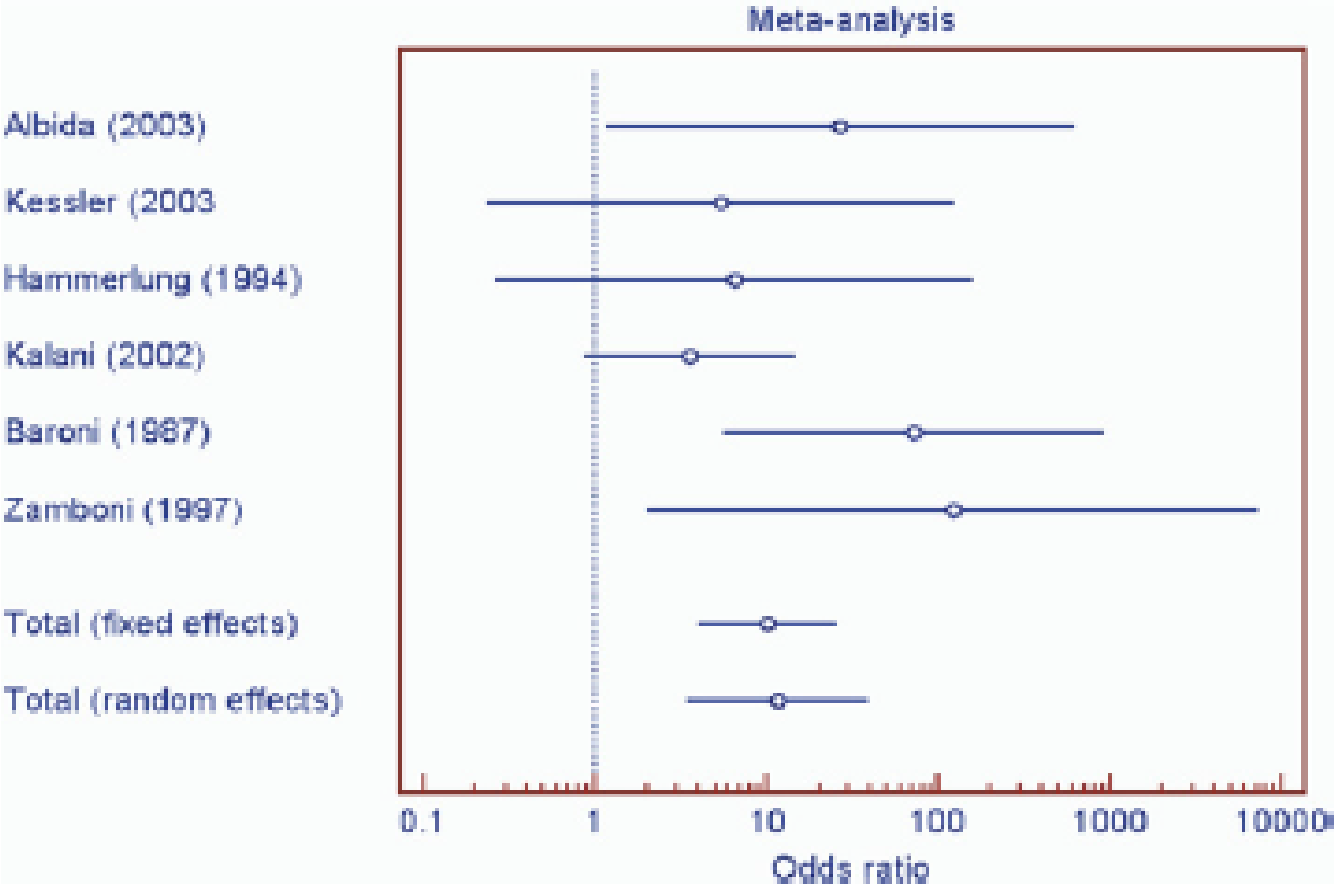
Hyperbaric Oxygen Therapy for Diabetic Foot Wounds, Benjamin A. Lipsky, Diabetes Care 2010 May; 33(5): 1143-1145.

Odds of DF amputation as a result of HBOT versus standard care



Hyperbaric oxygen therapy for wound healing and limb salvage: a systematic review. PM R. 2009 May;1(5):471-89. doi: 10.1016/j.pmrj.2009.03.012.

Odds of Healing of DF ulcer as a result of HBOT versus standard care



Hyperbaric oxygen therapy for wound healing and limb salvage: a systematic review. PM R. 2009 May;1(5):471-89. doi: 10.1016/j.pmrj.2009.03.012.

Hyperbaric oxygen …

ADA 2018, Recommendation

Ozone Therapy

- **Oxidative stress** is suggested to have an important role in the development of complications in diabetes.
- Because ozone therapy can activate the **antioxidant** system, influencing the level of glycemia and some markers of endothelial cell damage.

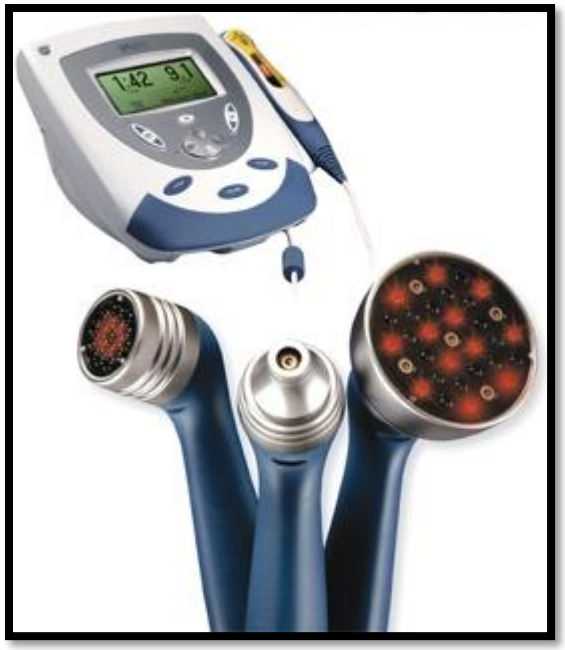
Therapeutic efficacy of ozone in patients with diabetic foot
Gregorio Martínez-Sánchez and etc., European Journal of Pharmacology
Volume 523, Issues 1–3, 31 October 2005, Pages 151–161

Negative pressure wound therapy

- Use to achieve closure of postoperative diabetic foot wounds
- To apply NPWT on wounds that have been thoroughly debrided and do not contain slough or necrotic tissue.
- The pump applies continuous negative pressure of 125 mmHg through a tube.

Laser therapy

LLLT is an effective modality to facilitate wound contraction in patients suffering from diabetes and used as an adjunct to conventional mode of treatment (dressings and debridement) for healing DFU.



Efficacy of Low Level Laser Therapy on Wound Healing in Patients with Chronic Diabetic Foot Ulcers
Indian J Surg. 2012 Oct; 74(5): 359–363.

مقاله پژوهشی

لیزرپزشکی؛ ۱۳۸۸، دوره ۶، شماره ۲، صفحات: ۳۵-۳۱.

بررسی لیزر کم توان در درمان زخم مزمن پای دیابتی: ارزیابی کمی میکروبیولوژیک

نسیم کاشف[۱]
ابوالفضل شجاعی فر[۲]
غلامرضا اسماعیلی جاوید[۳]
محمدرضا مهاجری[٤]
راضیه رضایی[٥]
ملیحه سلامی[٦]
مریم قدسی[٤]
محسن فاتح[۷]

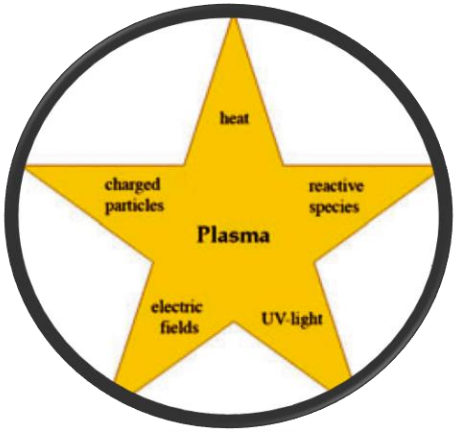
خلاصه

زمینه و هدف: دیابت ملیتوس یکی از بیماری های شایع در جهان و ایران می باشد. زخم پای دیابتی نیز یکی از عوارض شایع و ناتوان کننده بیماران مبتلا به دیابت به شمار می رود که روند ترمیم آن با تأخیر همراه بوده و می تواند به قطع عضو بیانجامد. روش های مختلفی برای تسریع بهبودی زخم مزمن پای دیابتی از جمله استفاده از تحریک زیست نوری یا لیزرهای کم توان معرفی شده است. با این حال هنوز مشخص نیست که بار میکروبی زخم (به عنوان یک عامل پیش آگهی ترمیم زخم) تحت تأثیر لیزر کم توان، چه تغییراتی خواهد داشت. هدف از انجام این فاز مطالعه، بررسی پایایی روش بررسی بار میکروبی و تأثیر اولیه درمان بر روی آن می باشد.

روش بررسی: بیماران مبتلا به زخم پای دیابتی با شدت وگنر ۱ الی ۳ وارد مطالعه شدند. پس از ارائه رضایت نامه، بیماران تحت درمان دبریدمان جراحی استاندارد، درمان آنتی بیوتیکی و حذف فشار قرار گرفتند. بیماران به طور تصادفی به دو گروه

Cold Plasma

- Hospital hygiene
- Antifungal treatment
- Dental care
- Skin disease
- Chronic wound
- Cosmetic
- Blood coagulation
- Pharmaceutical process
- Cancer treatment
- Improvement of proliferation of human cells
- Triggering of apoptosis on cells



Plasma-Stimulated Wound Healing

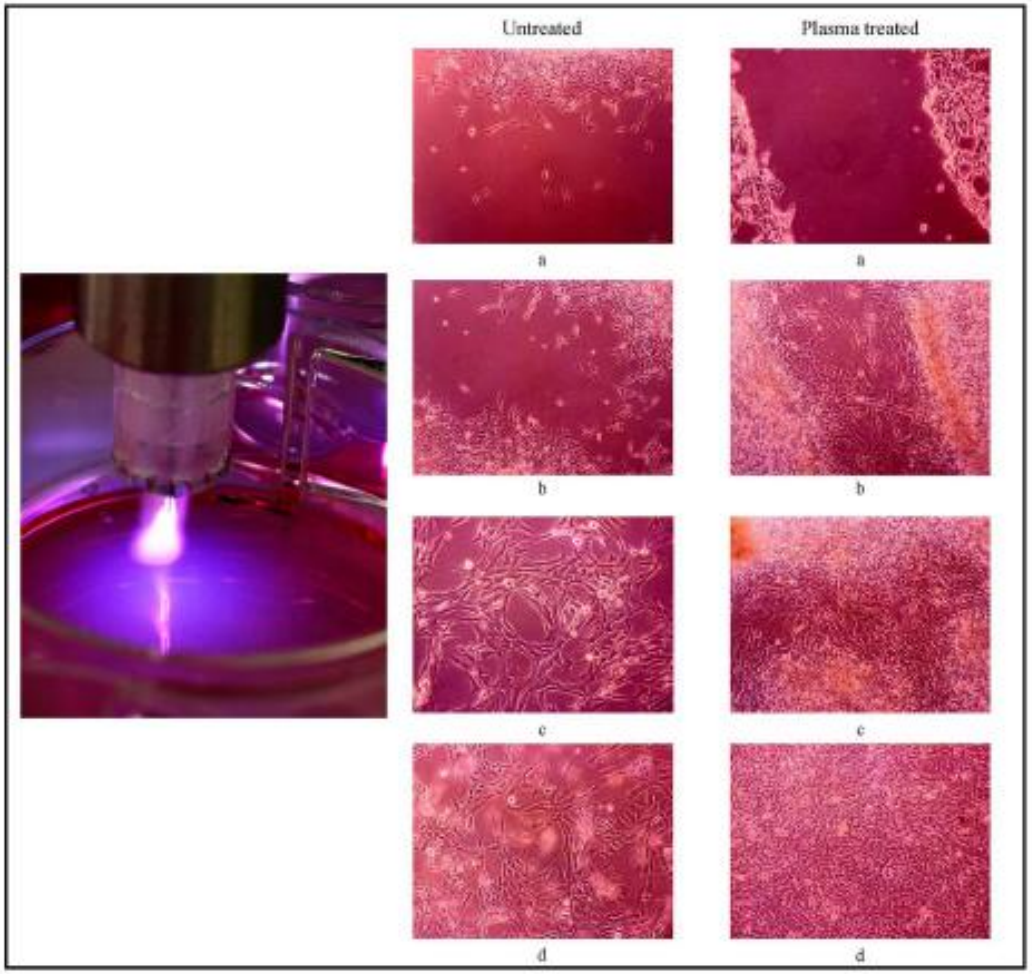
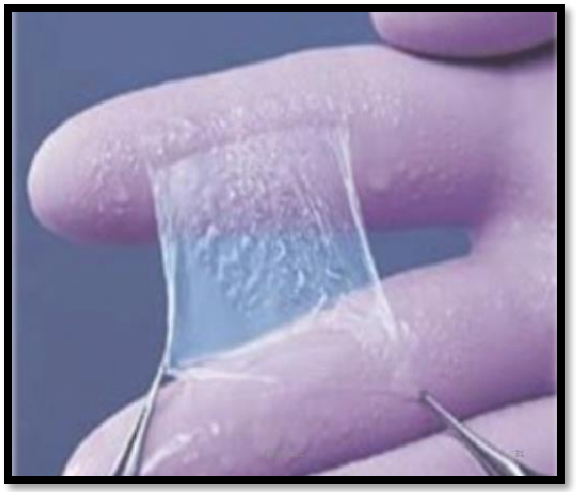


Fig. 1. In the left, a photograph of the plasma needle in contact with a cell culture is presented. The first column of microscope pictures represents the untreated samples, and the second column represents the plasma-treated samples. For the rows, picture *a* is taken immediately after the scratch was made, *b* after one day of incubation, *c* after two days of incubation, and *d* after three days of incubation.

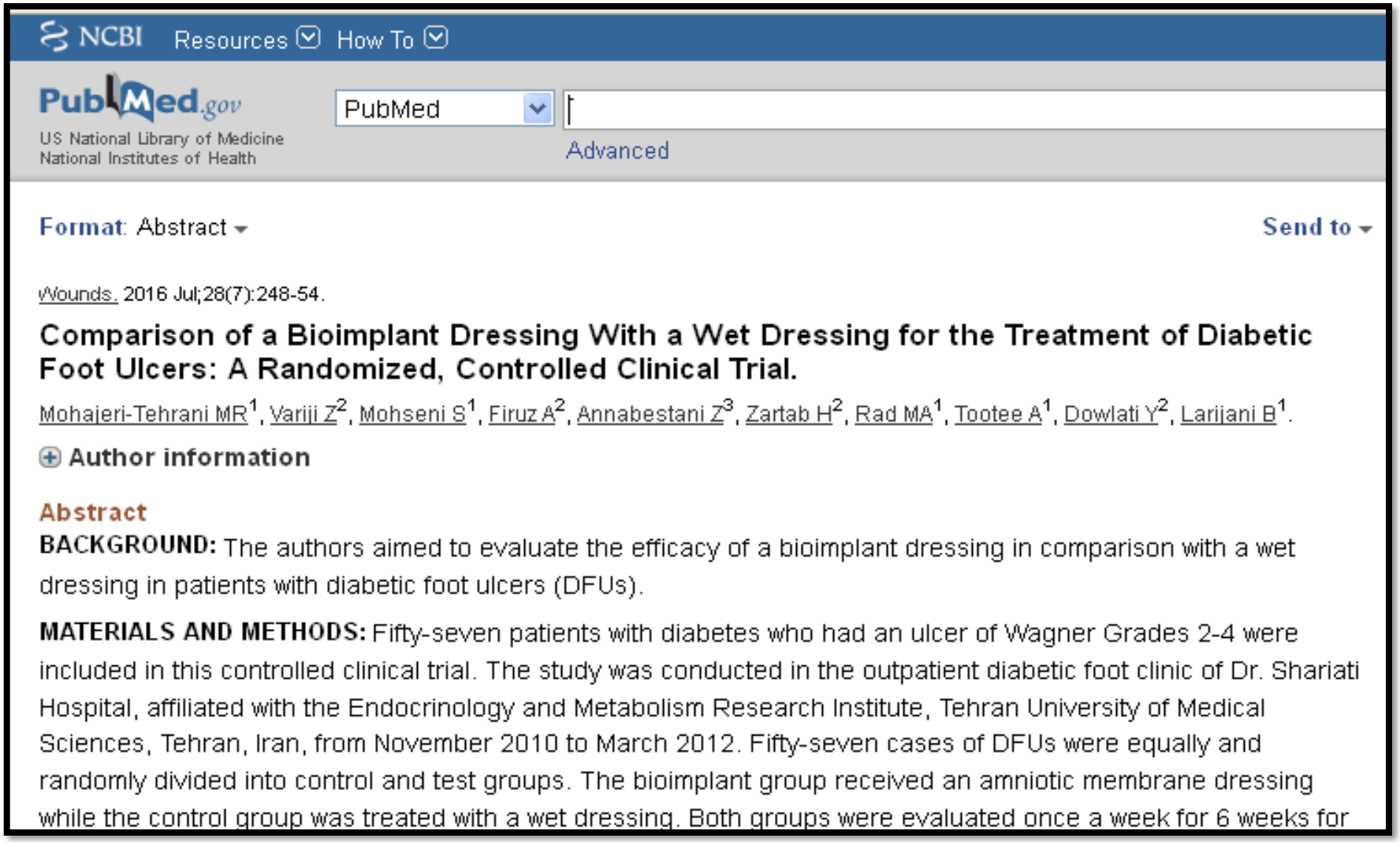
IEEE TRANSACTIONS ON PLASMA SCIENCE, VOL. 39, NO. 11, NOVEMBER 2011

Bioimplant



- The bioimplant dressing was significantly superior to the wet dressing in prompting the complete healing of DFUs.
- Ease of use, absence of adverse effects, and a facilitated wound healing process are among properties of amniotic membrane that make it an appropriate dressing in the management of DFUs.

Comparison of a Bioimplant Dressing With a Wet Dressing for the Treatment of Diabetic Foot Ulcers: A Randomized, Controlled Clinical Trial. Wounds. 2016 Jul;28(7):248-54.



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Wounds. 2016 Jul;28(7):248-54.

Comparison of a Bioimplant Dressing With a Wet Dressing for the Treatment of Diabetic Foot Ulcers: A Randomized, Controlled Clinical Trial.

Mohajeri-Tehrani MR[1], Variji Z[2], Mohseni S[1], Firuz A[2], Annabestani Z[3], Zartab H[2], Rad MA[1], Tootee A[1], Dowlati Y[2], Larijani B[1].

Author information

Abstract

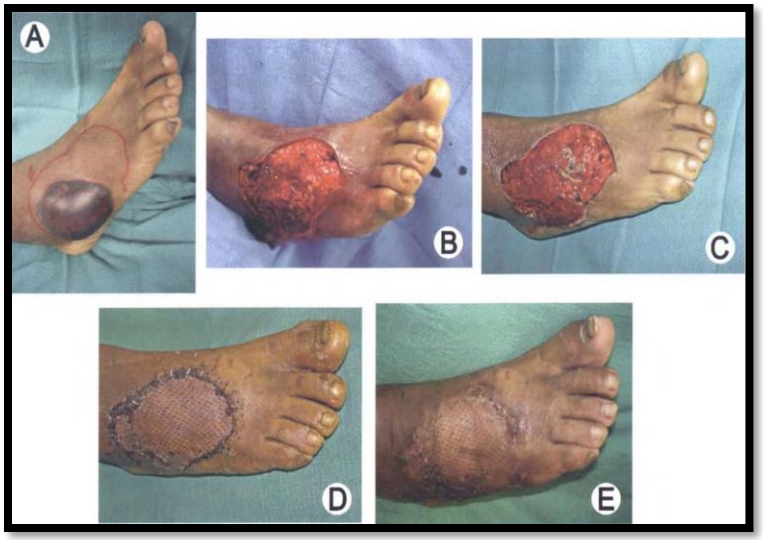
BACKGROUND: The authors aimed to evaluate the efficacy of a bioimplant dressing in comparison with a wet dressing in patients with diabetic foot ulcers (DFUs).

MATERIALS AND METHODS: Fifty-seven patients with diabetes who had an ulcer of Wagner Grades 2-4 were included in this controlled clinical trial. The study was conducted in the outpatient diabetic foot clinic of Dr. Shariati Hospital, affiliated with the Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran, from November 2010 to March 2012. Fifty-seven cases of DFUs were equally and randomly divided into control and test groups. The bioimplant group received an amniotic membrane dressing while the control group was treated with a wet dressing. Both groups were evaluated once a week for 6 weeks for

Skin & Artificial Skin Graft

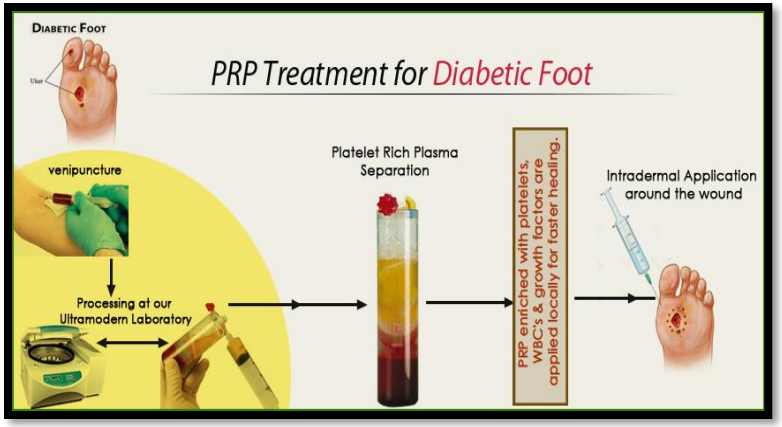
- To speed the healing of ulcers which have a clean granulating wound bed, a split skin graft may be harvested and applied to the ulcer.

- Apligraf and Dermagraf



Platelet Rich Plasma

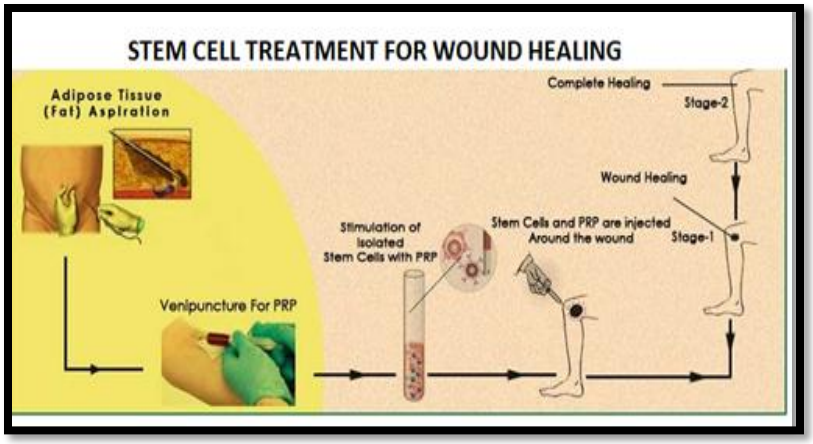
PRP is an autologous source of platelet-derived growth factor and transforming growth factor beta that is obtained by sequestering and concentrating platelets by gradient density centrifugation.



Treatment of a Non-Healing Diabetic Foot Ulcer With Platelet-Rich Plasma, Deepak H Suresh and etc, J Cutan Aesthet Surg. 2014 Oct-Dec; 7(4): 229–231.

Stem Cell Therapy

- Stem cells as a promising treatment for DFUs
- Capable of targeting, bypassing, the underlying abnormal healing mechanisms
- Deranged cell signaling in DFU and promote healing.



The role of stem cells in the treatment of diabetic foot ulcers. Diabetes Res Clin Pract. 2012 Apr;96(1):1-9.

Therapeutic Outcomes of Transplanting Autologous Granulocyte Colony-stimulating Factor-mobilised Peripheral Mononuclear Cells in Diabetic Patients with Critical Limb Ischaemia

Authors: L. Mohammadzadeh[1], S. H. Samodanifard[1], A. Keshavarzi[1], K. Alimoghaddam[1], B. Larijani[1], A. Ghavamzadeh[1], A. S. Ahmadi[1], A. Shojaeifard[1], M. R. Ostadali[2], A. M. Sharifi[4], M. R. Amini[2], A. Mahmoudian[3], H. Fakhraei[2], M. Aalaa[2], M. R. Mohajeri-Tehrani[2]

Affiliations: Affiliation addresses are listed at the end of the article

Key words
- peripheral arterial disease
- critical limb ischemia
- stem cell transplantation

Abstract

The efficacy and safety of transplanting autologous mesenchymal stem cells (MSCs), from granulocyte-colony-stimulating factor (G-CSF)-mobilised peripheral blood, was investigated in diabetic patients with critical limb ischaemia (CLI).

After 3 months, the transplanted group of patients cantly improved (P=0.035 and P=0.01, respectively).

Importantly, 50% of the control group (7/14 patients) faced major amputation of a limb at the study's conclusion, compared to none of 7 patients in the transplanted group (P=0.047).The safety of transplantation was confirmed by observing no adverse reactions among the trans-

Recovery index	Control group (n = 14)	Transplanted group (n = 7)	P-value*
major amputation, %	50 (n = 7)	0.0 (n = 0)	0.047
improvement in walking ability, %	28.6 (n = 4)	85.7 (n = 6)	0.024
improved blood flow, %	21.4 (n = 3)	100 (n = 7)	0.010
ABI measurement (mean ± SD)	0.65 ± 0.25	0.92 ± 0.15	0.035
peripheral neuropathy score† (mean ± SD)	6.77 ± 2.04	8.14 ± 1.21	0.140
wound size (mean ± SD), cm^2	18.16 ± 23.20	8.50 ± 6.15	0.290

* P-values were determined using Mann-Whitney, Chi-square and Fisher's exact tests

† Peripheral neuropathy scored by using monofilament examination

Table 2 Recovery indications at 3 months post-treatment.

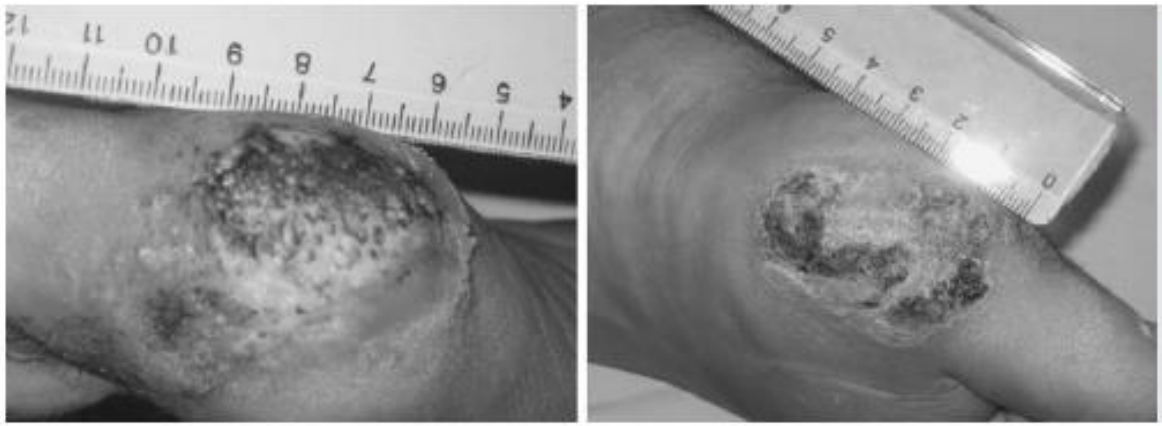


Fig. 2 Photos showing improvement in wound healing of diabetic foot ulcers before (left) and 3 months after transplantation (right).

ANGIPARSTM

- ✓ No side effects
- ✓ Can be used in all types of diabetic ulcers
- ✓ Decreased mean duration of hospital stay
- ✓ Decreased direct and indirect costs
- ✓ Decreased amputation rate

Biomolecular Research & Therapeutics

Aalaa et al., J Biomol Res Ther 2012, 1:2
http://dx.doi.org/10.4172/2167-7956.1000e104

Editorial Open Access

Smelil (ANGIPARS™) as a New Herbal Drug on Diabetic Foot Ulcer

Aalaa M, Heshmat R, Larijani B and Mohajeri-Tehrani MR*

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Introduction

Diabetes Mellitus is a most common metabolic disease in the world cause around 15% of diabetic patients suffer from Diabetic Foot Ulcer (DFU) in which 15-20% will lead to amputation [1,2]. Regardless of different types of diabetic foot ulcer treatment the incidence of lower extremities amputation among diabetics is still high [3]. In this regard ANGIPARS™ as a novel safe herbal formulation has been presented for diabetic foot ulcer. Results of studies which evaluate the effectiveness the main substance (Melilotus) of this product revealed not only it is effective in elimination of skin aging and stimulate microvascularization but also it has anti-inflammatory effects [4,5].

Clinical Trial Studies

Preclinical, experimental study

In this phase, the acute toxicity, genotoxicity, apoptotic effects, sub acute toxicity, mutagenic effects, fetal toxicity, and allergic effects of ANGIPARS™ have been evaluated and there was not any acute or chronic toxicity so that it was recommended for clinical studies [6,7].

Phase IV clinical trial study (Post-marketing)

In Post-Marketing study patients administered 100 mg of ANGIPARS™ capsules orally twice a day plus topical 3% gel for 45 days. Mean ulcer surface area considerably decreased. In addition there was a significant rise in Ankle Brachial Index (ABI) and Toe Brachial Index (TBI) after treatment period. It should be noted that there was not any significant side effects or toxicity during the Post-Marketing study.

Conclusion

ANGIPARS™ as a novel herbal formulation, presented for treatment of diabetic foot ulcer. Taking into account the efficacy and safety of ANGIPARS™ which has evaluated through multicentre double blind placebo controlled phases of trials and its very few toxic effects, effectiveness in diabetic foot ulcer healing, decreasing wound size along with enhancing microvascularization, it could be recommended in diabetic foot ulcer treatment. On the other word ANGIPARS™ along with other modality could be helpful in diabetic foot ulcer treatment especially when other treatments have not been effective. Finally it should be noted that use of ANGIPARS™ along with other treatments and debride-

Home Care Service Compared to Hospital Based Care for Diabetic Foot Patients

Table 2: characteristic of DF ulcers			
Variables		Hospital Care (N=90)	Home care (N=30)
Type of wound	Ischemic	15 (15%)	5 (16%)
	Nouroischemic	19 (19%)	10 (30%)
	Nouropathy	59 (60%)	14 (46%)
	Vein ulcer	5 (5%)	2 (6%)
Severity of ulcer	Wagner 2	46 (51%)	8 (26%)
	Wagner 3	28 (31%)	19 (63%)
	Wagner 4	16 (17%)	3 (1%)
Sepsis	Mild	19	3
	Moderate	32	6
	Sever	19	3
Home care follow up (Days)		-	21
Area ulcer (P value)		0.69	0.003*

*Significant

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Table 3 : Outcome indicator in participants included home care VS hospital care

	Control group (n= 90)	Intervention group (n= 30)	P
reduction in ulcer area (mm2) (mean, SD)	(-65.05 ,361.5)	(-256. 445.2)	<0.001
Rate of healed N (%)	28 (31%)	20 (66%)	0.01
Rate of amputation N (%)	16 (%17)	0 (0)	0.01
Rate of Death by 6 months N (%)	15 (%16)	6 (%20)	0.6
Rate of Unhealed N (%)	30 (33%)	4 (13%)	0.03
Length of stay (days) Mean (SD)	20.3 (14.5)	21 (1.01)	0.7

Conclusion

- Diabetic foot-related problems occur frequently and may have serious consequences.
- Standard treatment of DF ulcer is cornerstone of patients management.
- Although novel therapy of DF ulcer help us to accelerate ulcer healing.

EMRI Diabetic Foot Research Group