Analysts and Investor Day
EscharEx® - Enzymatic Debridement Agent for Chronic Wounds

March 30, 2021 I Nasdaq: MDWD

Cautionary Note Regarding Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of Section 27A of the U.S. Securities Act of 1933, as amended, Section 21E of the U.S. Securities Exchange Act of 1934, as amended and the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. We make forward-looking statements in this presentation that are subject to risks and uncertainties. These forward-looking statements include information about possible or assumed future results of our business, financial condition, results of operations, liquidity, plans and objectives. In some cases, you can identify forward-looking statements by terminology such as “believe,” “may,” “estimate,” “continue,” “anticipate,” “intend,” “should,” “plan,” “expect,” “predict,” “potential,” or the negative of these terms or other similar expressions. Forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. You should not unduly rely on any forward-looking statements. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that future results, levels of activity, performance and events and circumstances reflected in the forward-looking statements will be achieved or will occur. The statements we make regarding the following matters, among others, are forward-looking by their nature: the timing and conduct of our trials of NexoBrid, EscharEx and our other pipeline product candidates, including statements regarding the timing, progress and results of current and future preclinical studies and clinical trials, and our research and development programs; the clinical utility, potential advantages and timing or likelihood of regulatory filings and approvals of NexoBrid, EscharEx and our pipeline products; our plans to develop and commercialize NexoBrid, EscharEx and our pipeline product candidates; anticipated funding under our contracts with the U.S. Biomedical Advanced Research and Development Authority; our expectations regarding future growth, including our ability to develop new products; our commercialization, marketing and manufacturing capabilities and strategy and the ability of our marketing team to cover regional burn centers and units; our ability to maintain adequate protection of our intellectual property; our estimates regarding the market opportunity for NexoBrid and EscharEx and our pipeline products candidates; the impact of our research and development expenses aw we continue developing products candidates and the impact of laws and regulations. Actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of several important factors. In particular, you should consider: the uncertain, lengthy and expensive nature of the product development process; the timing and conduct of our trials of NexoBrid, EscharEx and our other pipeline product candidates, including the timing, progress and results of current and future preclinical studies and clinical trials, and our research and development programs; risks related to our collaboration with Vericel; our ability to obtain marketing approval of NexoBrid and EscharEx in the U.S. or other markets; the clinical utility, potential advantages and timing or likelihood of regulatory filings and approvals of NexoBrid, EscharEx and our pipeline products; our expectations regarding future growth, including our ability to develop new products; our commercialization, marketing and manufacturing capabilities and strategy and the ability of our marketing team to cover regional burn centers and units; risks related to our contract with the U.S. Biomedical Advanced Research and Development Authority; market acceptance of our products and product candidates; the possibility of unfavorable pricing regulations or lack of coverage by third parties and reimbursement policies; our operating expenses and history of net losses; our dependence on third party suppliers; our dependence on our manufacturing facility in Yavne, Israel and related manufacturing risks; our ability to maintain adequate protection of our intellectual property; side effects of our products and product candidates; competition risks; exchange rate fluctuations; litigation risks; risks related to our operations in Israel; our estimates regarding expenses, future revenues, capital requirements and the need for additional financing; the impact of government laws and regulations and the impact of the COVID-19 pandemic. Additional government-imposed quarantines and requirements to “shelter at home” or other incremental mitigation efforts also may impact our ability to source supplies for our operations or our ability or capacity to manufacture, sell and support the use of our products and product candidates in the future. These and other significant factors are discussed under the heading “Risk Factors” in our annual report on Form 20-F for the year ended December 31, 2020 as well as information contained in other documents filed with or furnished to the Securities and Exchange Commission. Any forward-looking statement made in this presentation speaks only as of the date hereof. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that future results, levels of activity, performance and events and circumstances reflected in the forward-looking statements will be achieved or will occur. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation, to conform these statements to actual results or to changes in our expectations.

Trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of the products or services of the Company. Certain data in this presentation, including the presentations of U.S. Wound Care treatment practice by Robert S. Kirsner, Market Research Insight by Ilina Sen, Comparator study in a pig model by Adam Singer and The Biofilm Opportunity by Robert J. Snyder, was obtained from various external sources, and neither the Company nor its affiliates, advisers or representatives has verified such data with independent sources. Accordingly, neither the Company nor any of its affiliates, advisers or representatives makes any representations as to the accuracy or completeness of that data or to update such data after the date of this presentation. Such data involves risks and uncertainties and is subject to change based on various factors..

Funding and technical support for development of NexoBrid including the expanded access treatment protocol (NEXT), the pivotal Phase 3 pediatric clinical study (CIDS) and the marketing approval registration process for NexoBrid in the U.S. as well as the development of NexoBrid for Mustard Sulfur injuries is provided by the Biomedical Advanced Research and Development Authority (BARDA), under the Assistant Secretary for Preparedness and Response (ASPR), within the U.S. Department of Health and Human Services (HHS), under ongoing USG Contract No. HHSO100201500035C and No. HHSO100201800023C. Additional projects for evaluation of NexoBrid funded under the BARDA contract include randomized, controlled pivotal clinical trial for use in adults population, establishment of a pre-emergency use data package and development of the health economic model to evaluate the cost savings impact to enable market adoption in the United States and readiness for emergencies.

We maintain our books and records in U.S. Dollar and report under International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board. None of the consolidated financial statements incorporated by reference into this prospectus supplement were prepared in accordance with generally accepted accounting principles in the United States.

The information contained herein does not constitute a prospectus or other offering document, nor does it constitute or form part of any invitation or offer to sell, or any solicitation of any invitation or offer to purchase or subscribe for, any securities of MediWound or any other entity, nor shall the information or any part of it or the fact of its distribution form the basis of, or be relied on in connection with, any action, contract, commitment or relating thereto or to the securities of MediWound.

Committed to innovation, we are dedicated to improving quality of care and patient lives

About Us

Innovative biopharmaceutical company

Focused on next-generation bio-therapeutic solutions for tissue repair and regeneration

Diversified and differentiated product portfolio

Clinically and commercially validated bio-active therapies targeting unmet medical needs in burn care, wound care, and tissue repair

Proprietary enzymatic platform technology

State-of-the-art, cGMP certified sterile manufacturing facility

Strong management with proven execution capabilities

Diversified Portfolio of Differentiated Product

NexoBrid

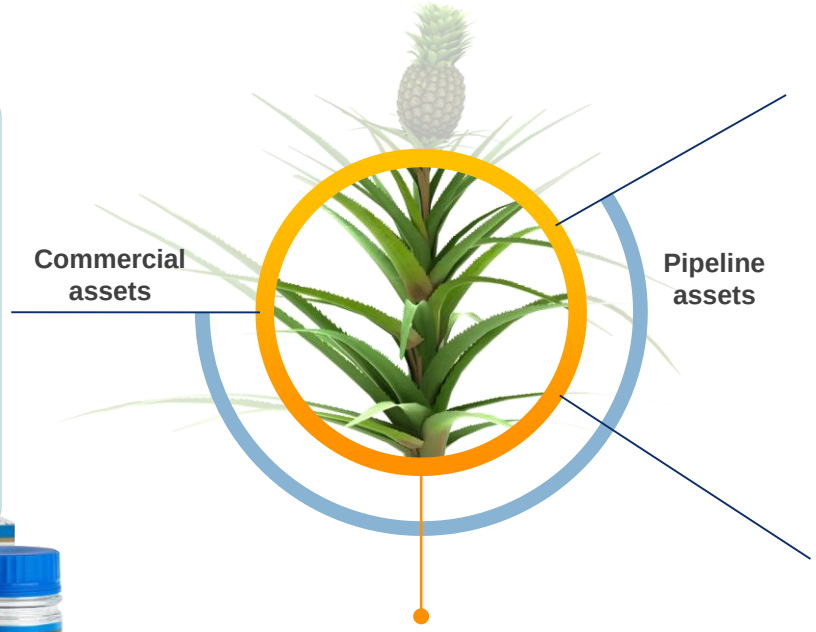
Next generation of burn care

Indication: Eschar removal of deep partial and full thickness burns

Classification: Biological orphan drug

Target audience: Hospitalized patients

Development status: EU and international market approvals in hand; BLA accepted for filing by the FDA, with a PDUFA goal date of June 29, 2021



A complex mixture of proteins derived from the pineapple stem, enriched in bromelain

EscharEx

Bioactive debridement agent

Indication: Debridement of chronic/hard-to-heal wounds (VLU's/DFU's/pressure ulcers)

Classification: Biological drug candidate

Target audience: Outpatient setting

Development status: U.S. Phase II adaptive design study underway

*Investigational Drug, not approved in any jurisdiction

MWPC005

Topical enzymatic biotherapy

Indication: Treatment of non-melanoma skin cancer

Classification: Biological drug candidate

Target audience: Outpatient setting

Development status: U.S. Phase I/II study initiation is planned for 2Q 2021

*Investigational Drug, not approved in any jurisdiction

Today's Agenda

Introduction

Sharon Malka, CEO, MediWound

Current Chronic Wounds Debridement Practice

Robert S. Kirsner, M.D., Ph.D., University of Miami

Market Landscape Analysis

Ilina Sen, Sr. Director, Huron Consulting Group

EscharEx In-vivo H-t-H Comparator Study

Adam J. Singer, M.D., Stony Brook University

The Biofilm Opportunity

Robert J. Snyder, D.P.M., M.Sc., Barry University

MediWound Business Update

Sharon Malka, CEO, MediWound

Experts Panel Discussion and Q&A

Robert S. Kirsner, M.D., PhD
Chairman & Harvey Blank Professor
Dr. Phillip Frost Department of Dermatology & Cutaneous Surgery
Professor of Public Health Sciences
Director, University of Miami Hospital and Clinics Wound Center
University of Miami Miller School of Medicine

Ilina Sen
Life Sciences Sr. Director,
Huron Consulting Group

Adam J. Singer MD
Professor and Vice Chairman for Research
Department of Emergency Medicine
Stony Brook University

Robert J Snyder, DPM, MBA, MSc, CWSP, FFPM RCPS (Glasg)
Interim Dean, Professor and Director of Clinical Research, Barry University SPM
Past President, Association for the Advancement of Wound Care
Past President, American Board of Wound Management

Current Chronic Wound Debridement Practices

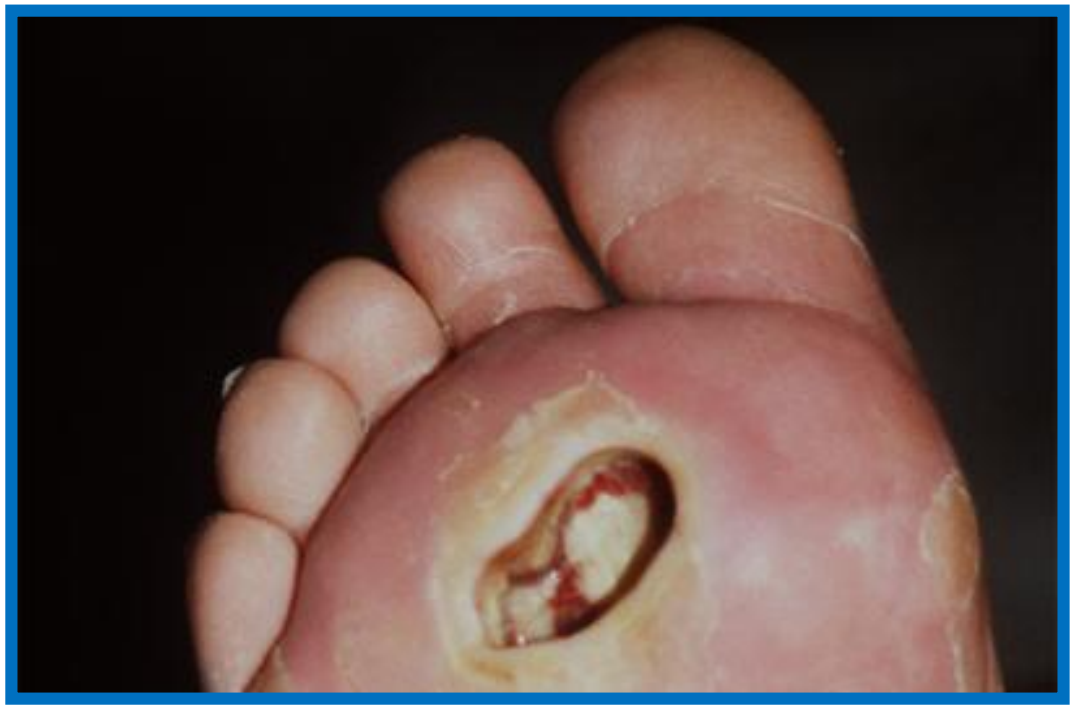
Robert S. Kirsner, M.D., PhD
Chairman & Harvey Blank Professor
Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery
University of Miami Miller School of Medicine
Miami, Florida

Brief Biography

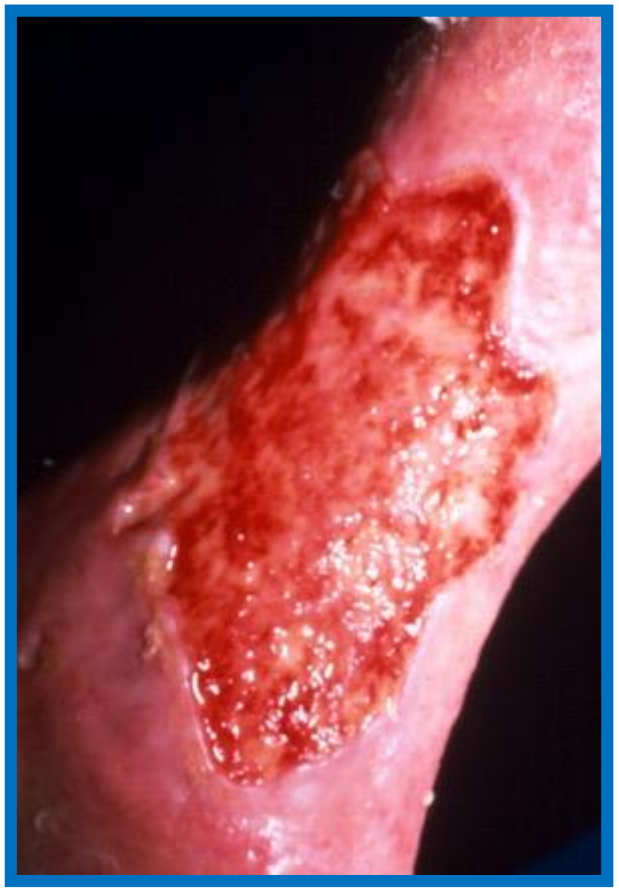
- **SAWC – Co-Chairperson 25+ years**
- **International Steering Committee – WUWHS**
- **Largest Wound Healing Research Program in US**
- **Former Head Advisory Committee – Largest WH Service Company in US**
- **Led Major RCTs, Clinical and Humanitarian Efforts**

The Clinical Problem

Diabetic Foot Ulcers



Venous Leg Ulcers



Common Chronic Wounds

High prevalence

High cost

High complications

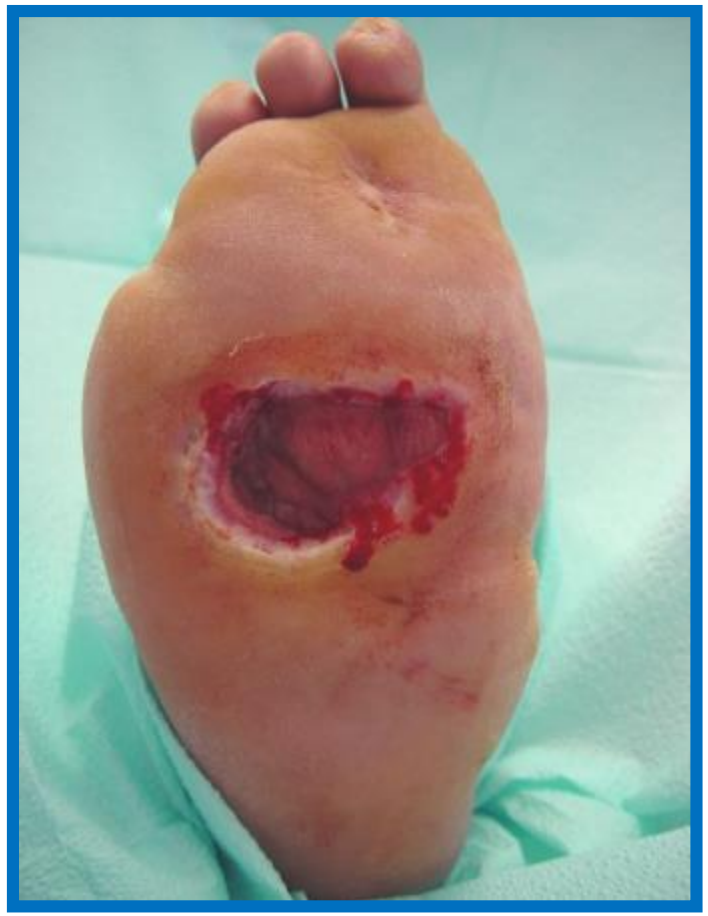
Impact of Chronic Wounds

Chronic wounds affect 6 million Americans each year

Cost > $40 billion

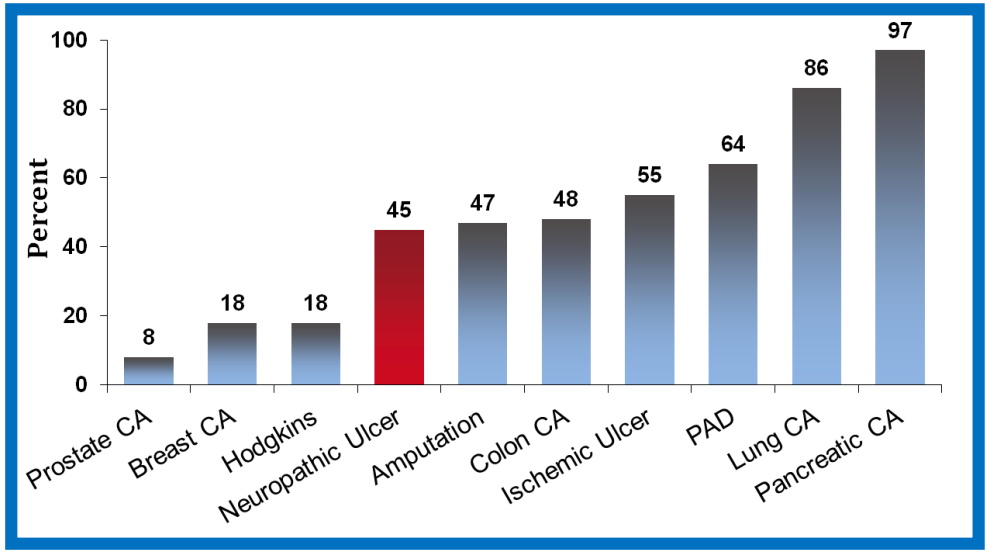
Sen et al: Wound Repair Regen. 2009;17(6):763-71

Mortality Rates



Diabetic Neuropathic Ulcer

Foot ulcers from diabetes have higher mortality rate (45% over 5 years) than many cancers, including breast and prostate!



Robbins JM, Strauss G, Aron D, Long J, Kuba J, Kaplan Y. J Am Podiatr Med Assoc. 2008 Nov-Dec

CA = carcinoma; PAD = peripheral artery disease.
Armstrong DG, et al. *Int Wound J*. 2007;4(4):286-287.

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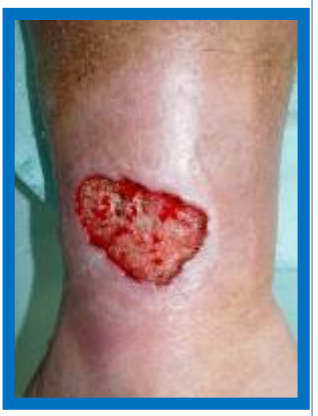
Burden of Disease



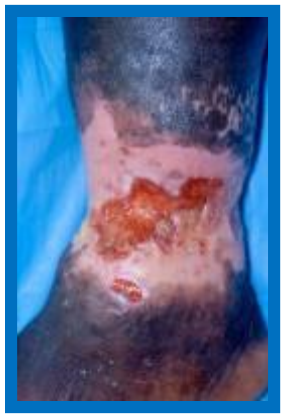
Original article

Burden of venous leg ulcers in the United States

Table 5. Estimated annual incidence of VLU in Medicare and private insurance.

	Medicare			Private insurance		
Year	New patients[a]	Total patients[b]	Incidence[c]	New patients[a]	Total patients[b]	Incidence[c]
2007	23,644	1,116,983	2.1%	8322	1,917,988	0.4%
2008	23,348	1,094,325	2.1%	7556	1,545,801	0.5%
2009	24,369	1,089,946	2.2%	7592	1,507,734	0.5%
2010	–	–	–	10,009	1,656,530	0.6%
Total	71,361	3,301,254	2.2%	33,479	6,628,053	0.5%

[a]New patients defined as those with at least one VLU diagnosis in the calendar year but no VLU diagnosis in the previous year. Patients were also required to meet other sample selection criteria (in terms of age restrictions and enrollment).
[b]Total patients were defined as those with at least one medical claim and continuous non-HMO insurance coverage in the year of estimation as well as the previous year.
[c]Incidence was calculated by dividing the number of new patients by the number of total patients in the calendar year.



Venous leg ulcers:
Prevalence = 2.2 million patients annually in US

VLU = venous leg ulcer.

Rice JB, et al. *J Med Econ*. 2014;17(5):347-356.
Singer AJ, Tassiopoulos A, Kirsner RS. N Engl J Med. 2017;377:1559-1567

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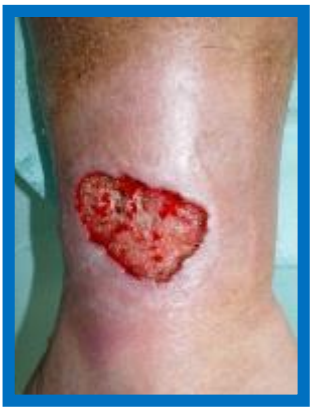
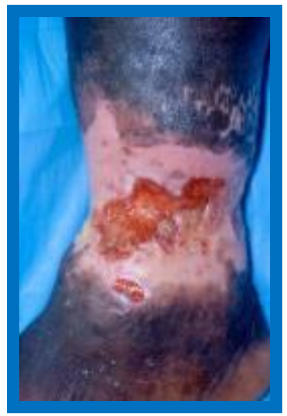
- Incremental costs of VLU: $6000-$7000
- Increased work loss days: 4 per patient
- Total incremental costs of VLU: $14.9B





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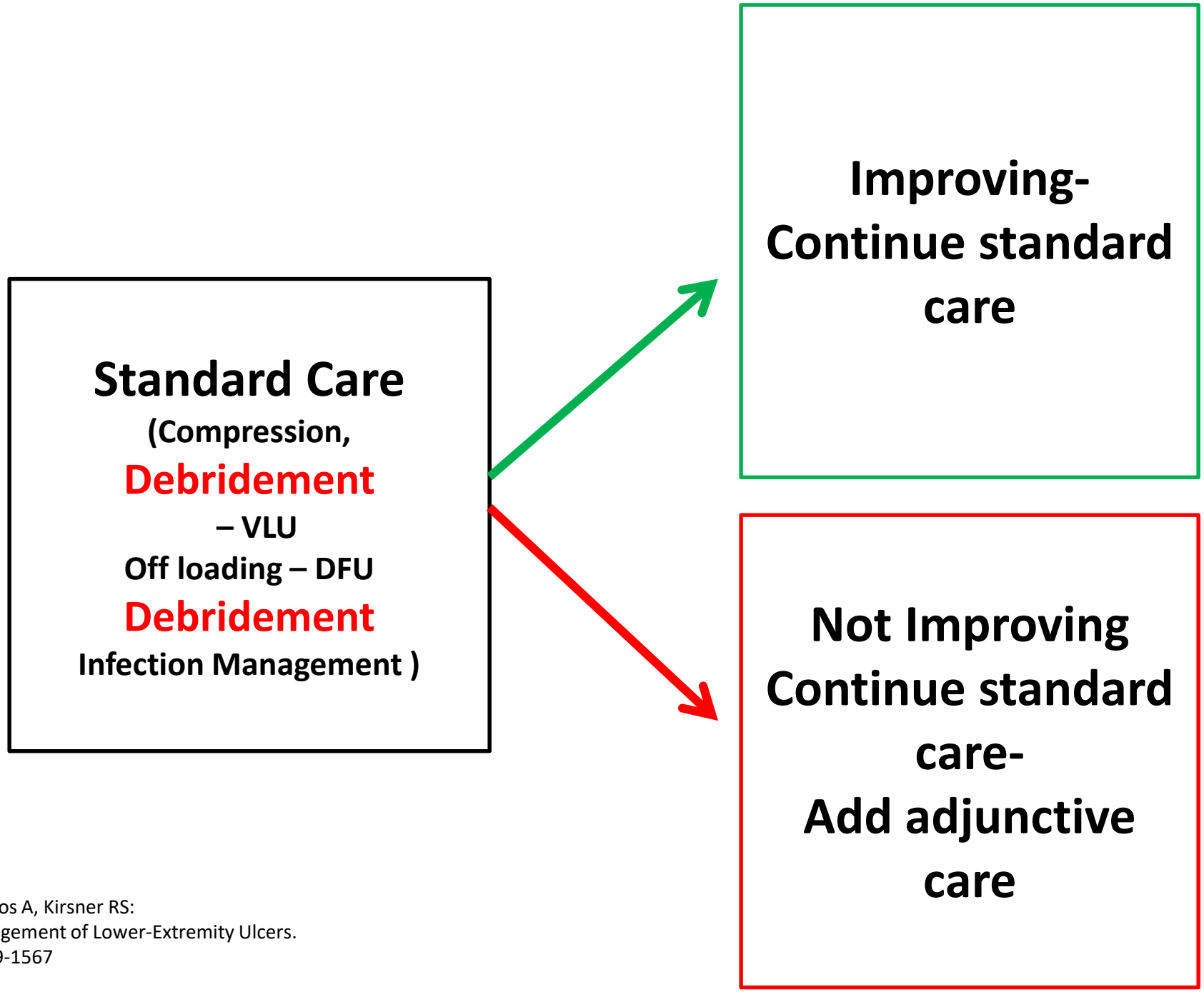
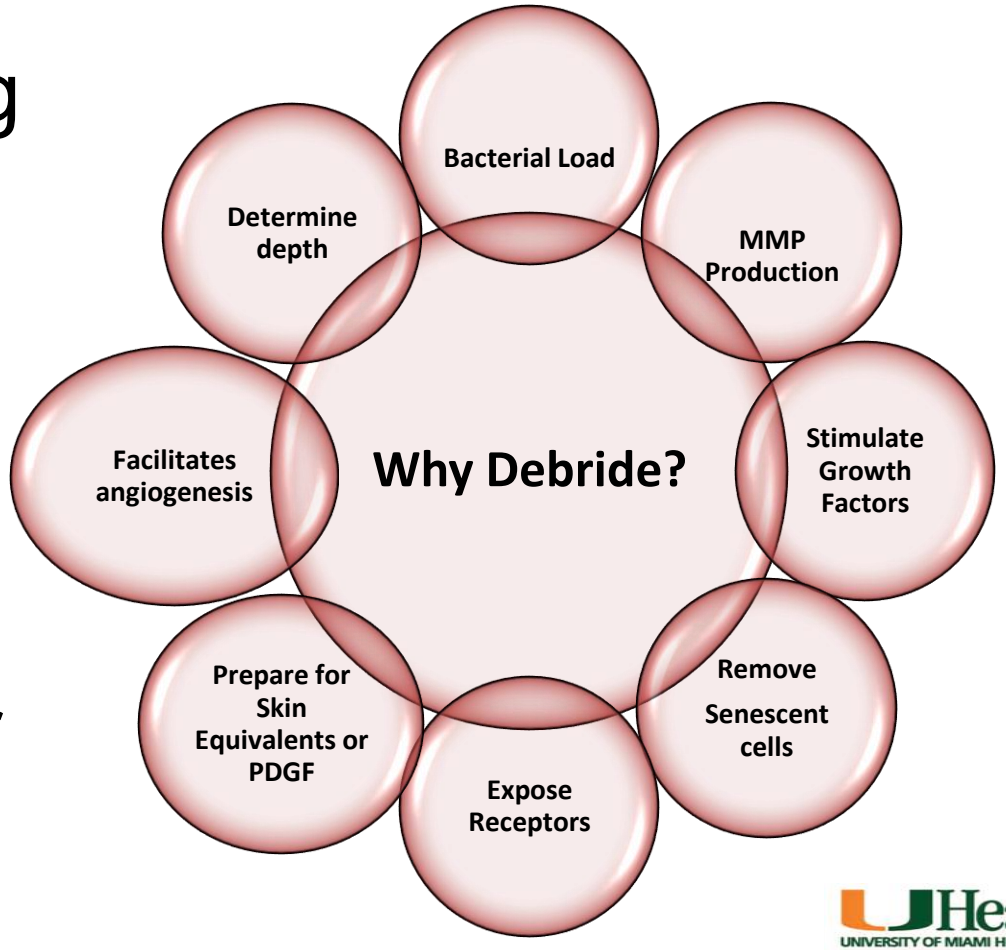


Singer AJ, Tassiopoulos A, Kirsner RS:
Evaluation and Management of Lower-Extremity Ulcers.
NEJM 2017:377:1559-1567

Goal of Debridement

- To remove necrotic tissue and to expose and stimulate functional dividing and migrating cells
- To reduce surface bioburden
- To reduce inflammatory/Proteolytic Environment
- To provide an environment where wound healing can occur



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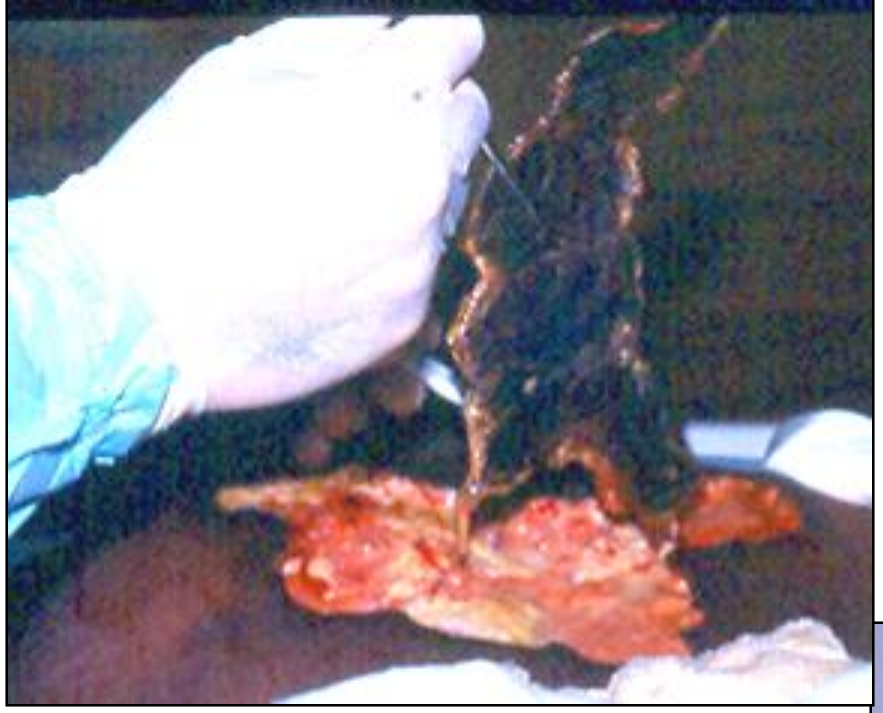
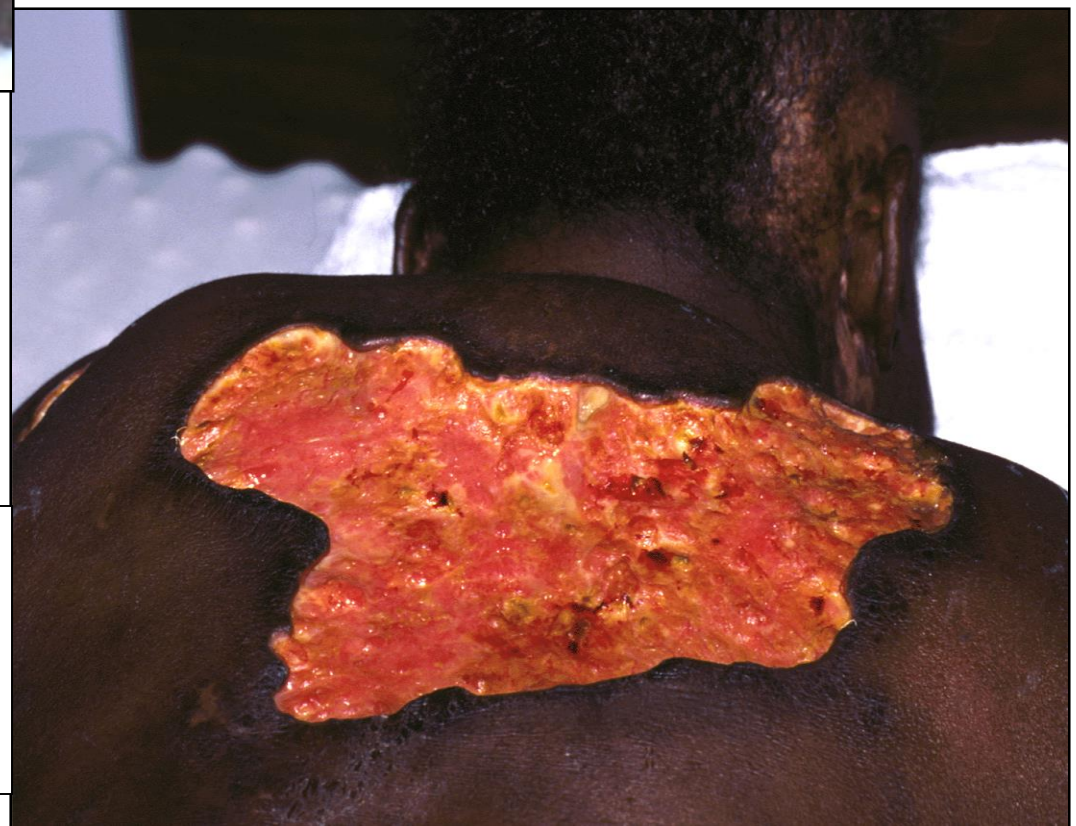


Outcome Desired
Removal of Necrotic Tissue

Mission Accomplished!!



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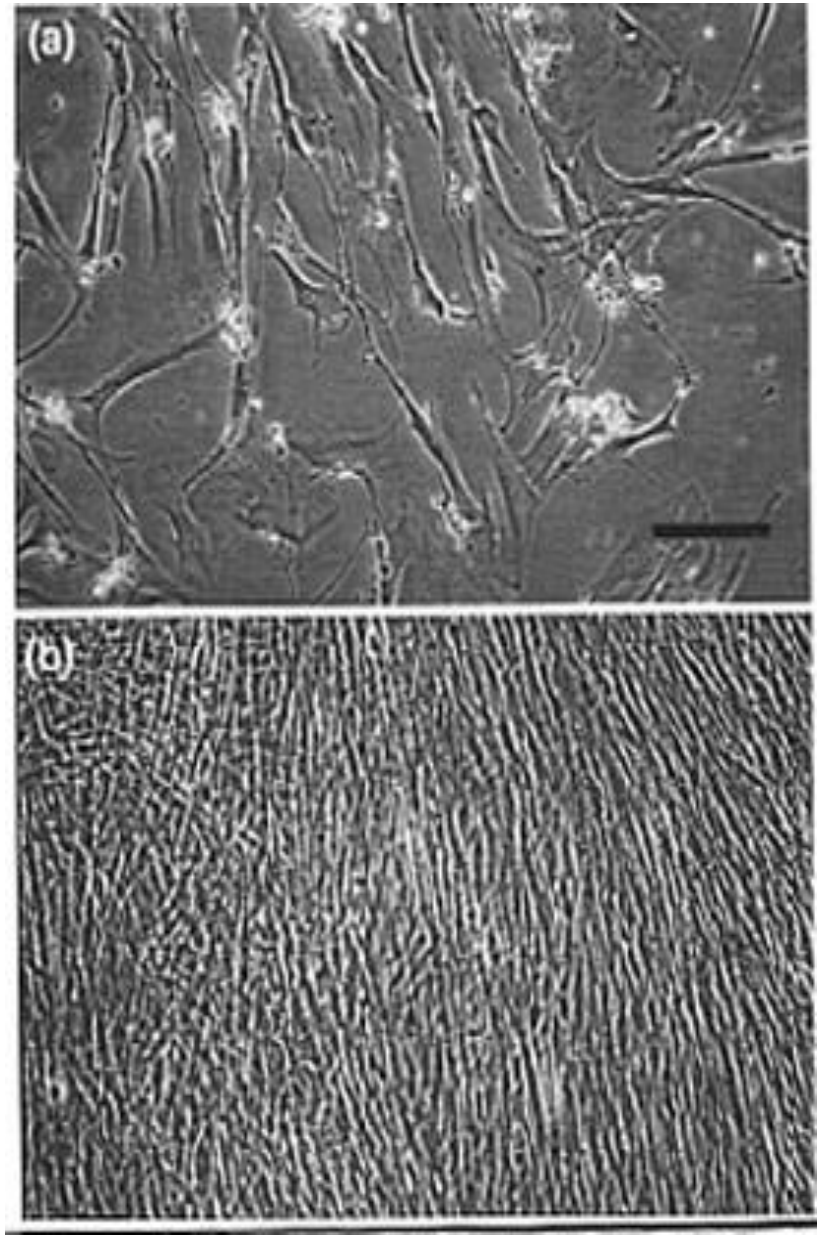
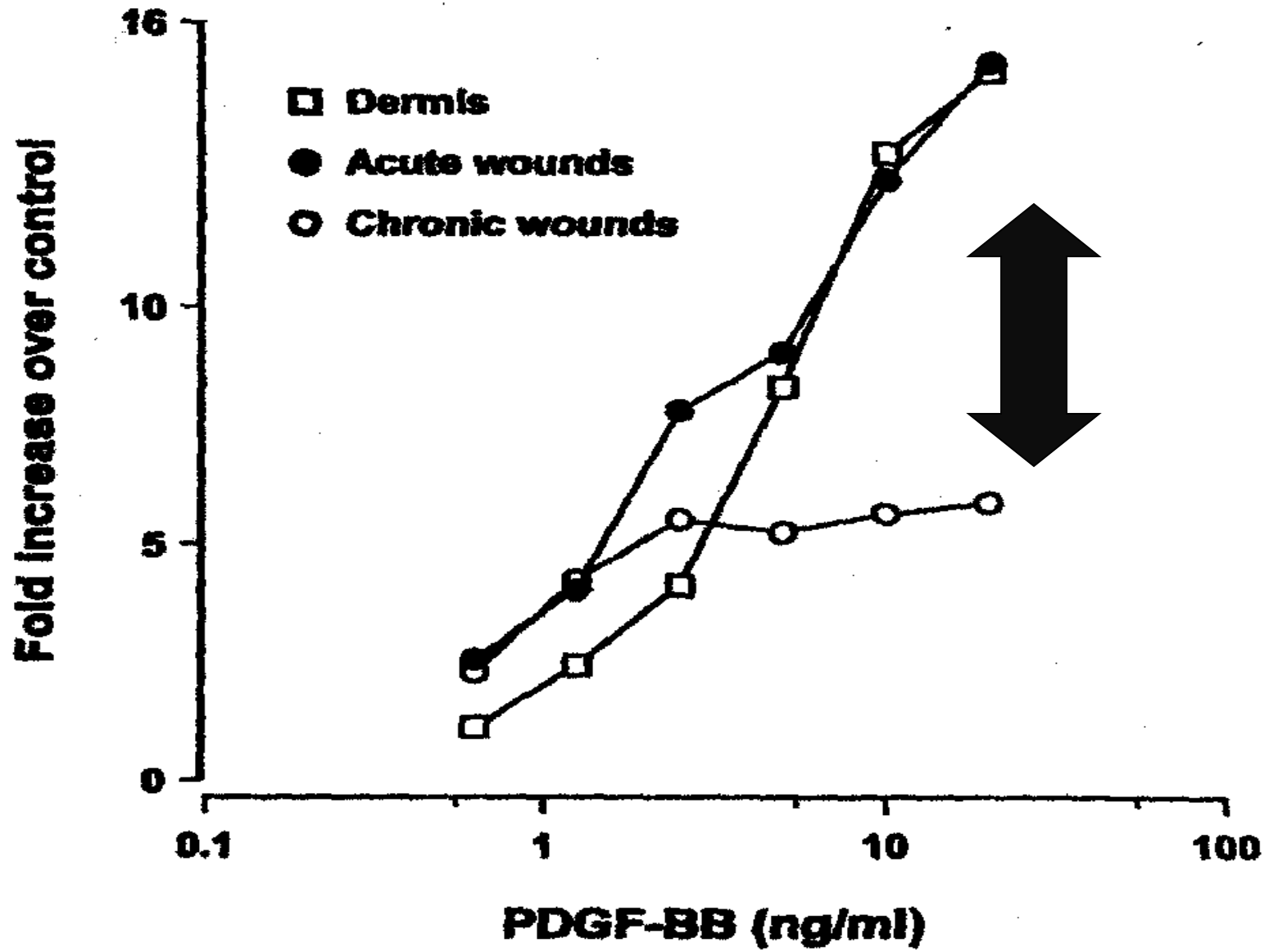
Fibroblasts - 10 days

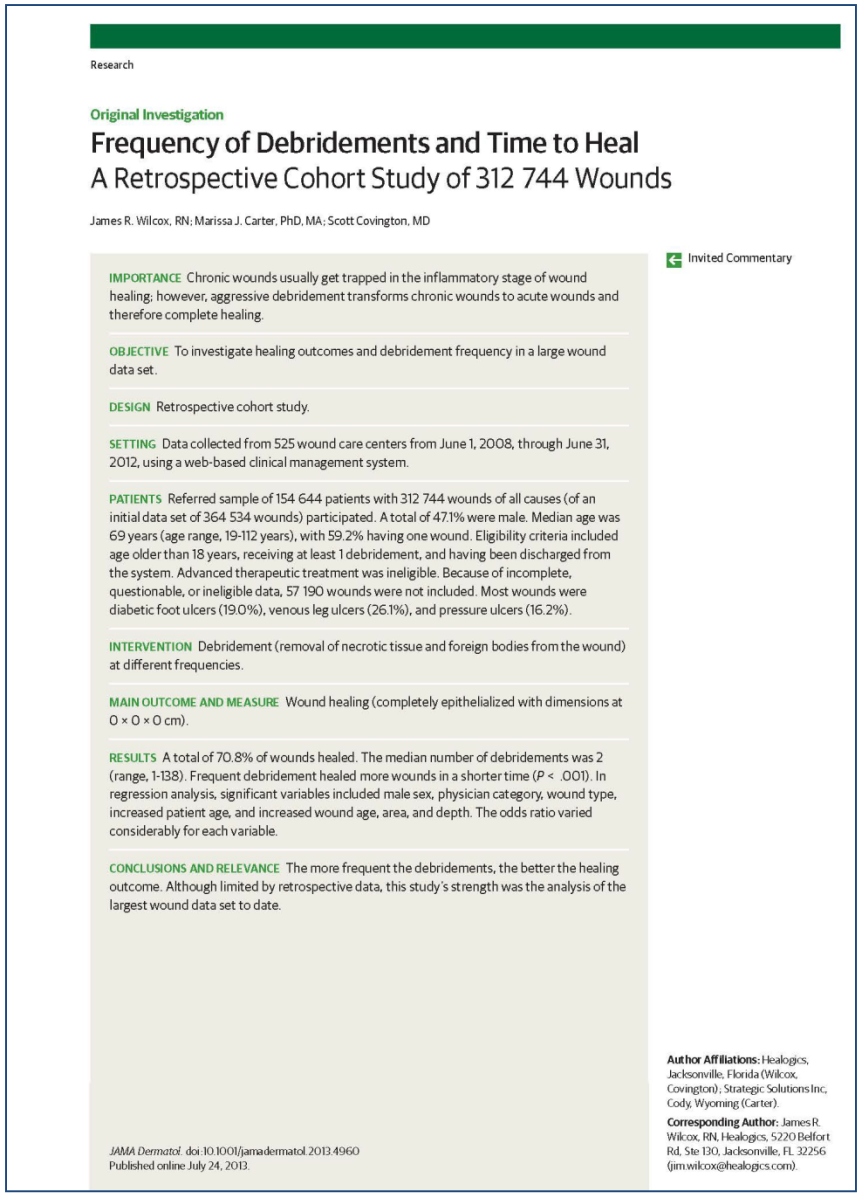
(a) Chronic Wound

(b) Acute Wound





Agren et al: J Invest Dermatol 1999



Research

Original Investigation

Frequency of Debridements and Time to Heal
A Retrospective Cohort Study of 312 744 Wounds

James R. Wilcox, RN; Marissa J. Carter, PhD, MA; Scott Covington, MD

Invited Commentary

IMPORTANCE Chronic wounds usually get trapped in the inflammatory stage of wound healing; however, aggressive debridement transforms chronic wounds to acute wounds and therefore complete healing.

OBJECTIVE To investigate healing outcomes and debridement frequency in a large wound data set.

DESIGN Retrospective cohort study.

SETTING Data collected from 525 wound care centers from June 1, 2008, through June 31, 2012, using a web-based clinical management system.

PATIENTS Referred sample of 154 644 patients with 312 744 wounds of all causes (of an initial data set of 364 534 wounds) participated. A total of 47.1% were male. Median age was 69 years (age range, 19-112 years), with 59.2% having one wound. Eligibility criteria included age older than 18 years, receiving at least 1 debridement, and having been discharged from the system. Advanced therapeutic treatment was ineligible. Because of incomplete, questionable, or ineligible data, 57 190 wounds were not included. Most wounds were diabetic foot ulcers (19.0%), venous leg ulcers (26.1%), and pressure ulcers (16.2%).

INTERVENTION Debridement (removal of necrotic tissue and foreign bodies from the wound) at different frequencies.

MAIN OUTCOME AND MEASURE Wound healing (completely epithelialized with dimensions at 0 × 0 × 0 cm).

RESULTS A total of 70.8% of wounds healed. The median number of debridements was 2 (range, 1-138). Frequent debridement healed more wounds in a shorter time ($P < .001$). In regression analysis, significant variables included male sex, physician category, wound type, increased patient age, and increased wound age, area, and depth. The odds ratio varied considerably for each variable.

CONCLUSIONS AND RELEVANCE The more frequent the debridements, the better the healing outcome. Although limited by retrospective data, this study's strength was the analysis of the largest wound data set to date.

JAMA Dermatol. doi:10.1001/jamadermatol.2013.4960
Published online July 24, 2013.

Author Affiliations: Healogics, Jacksonville, Florida (Wilcox, Covington); Strategic Solutions Inc, Cody, Wyoming (Carter).

Corresponding Author: James R. Wilcox, RN, Healogics, 5220 Belfort Rd, Ste 130, Jacksonville, FL 32256 (jim.wilcox@healogics.com).

N = 312,744 wounds
154,664 patients
525 WCC

4 yr. period (2008-2012)

Most Common Wound Types:
VLU 26.1%
DFU 19%
PU 16.2%

Avg. # of debridements = 2 (range 1-138)

J Wilcox et al. JAMA Dermatology. 2013; 149 (9): 1050-1058.

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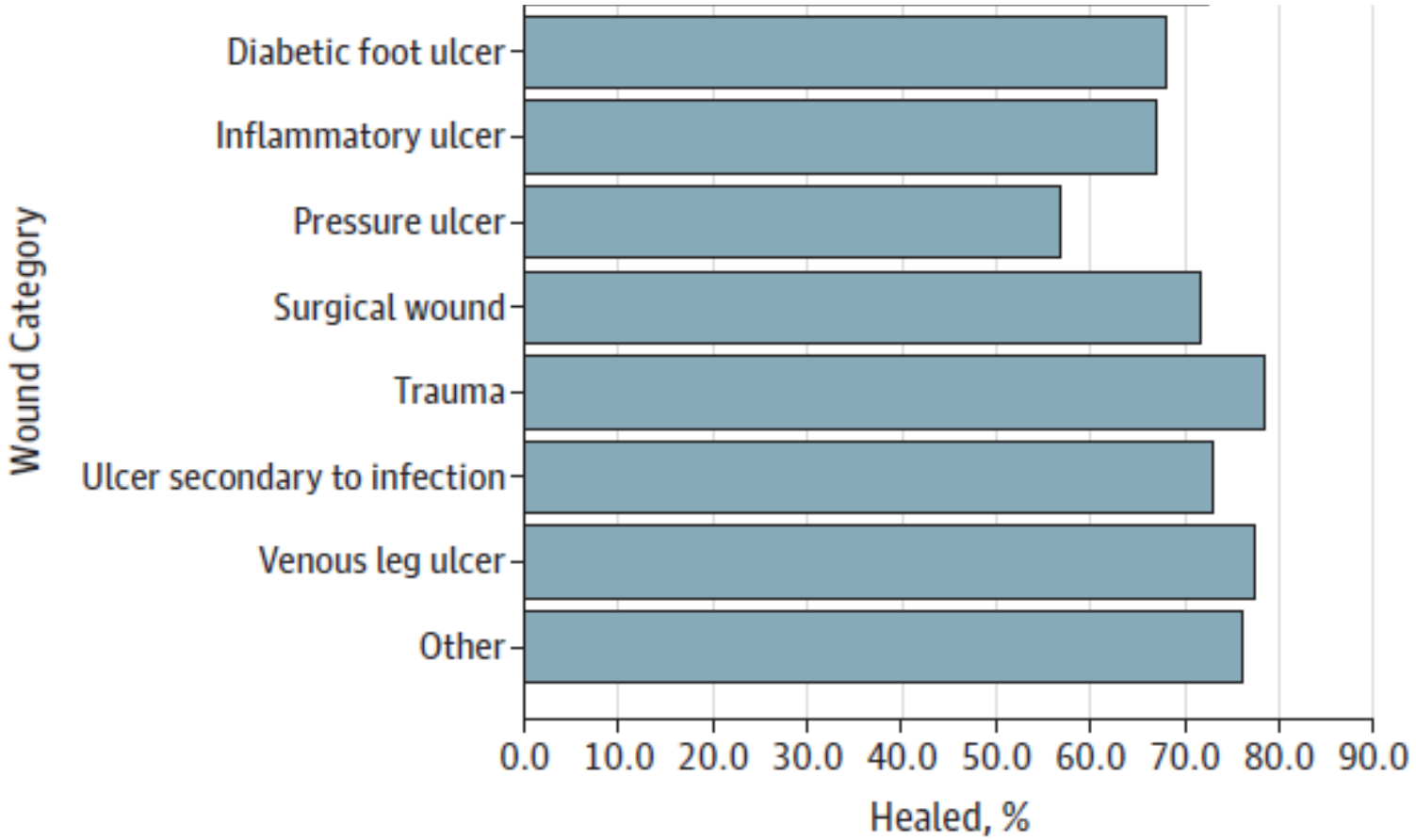

Healing Rates for the Different Categories of Wounds

J Wilcox et al. JAMA Dermatology. 2013; 149 (9): 1050-1058.

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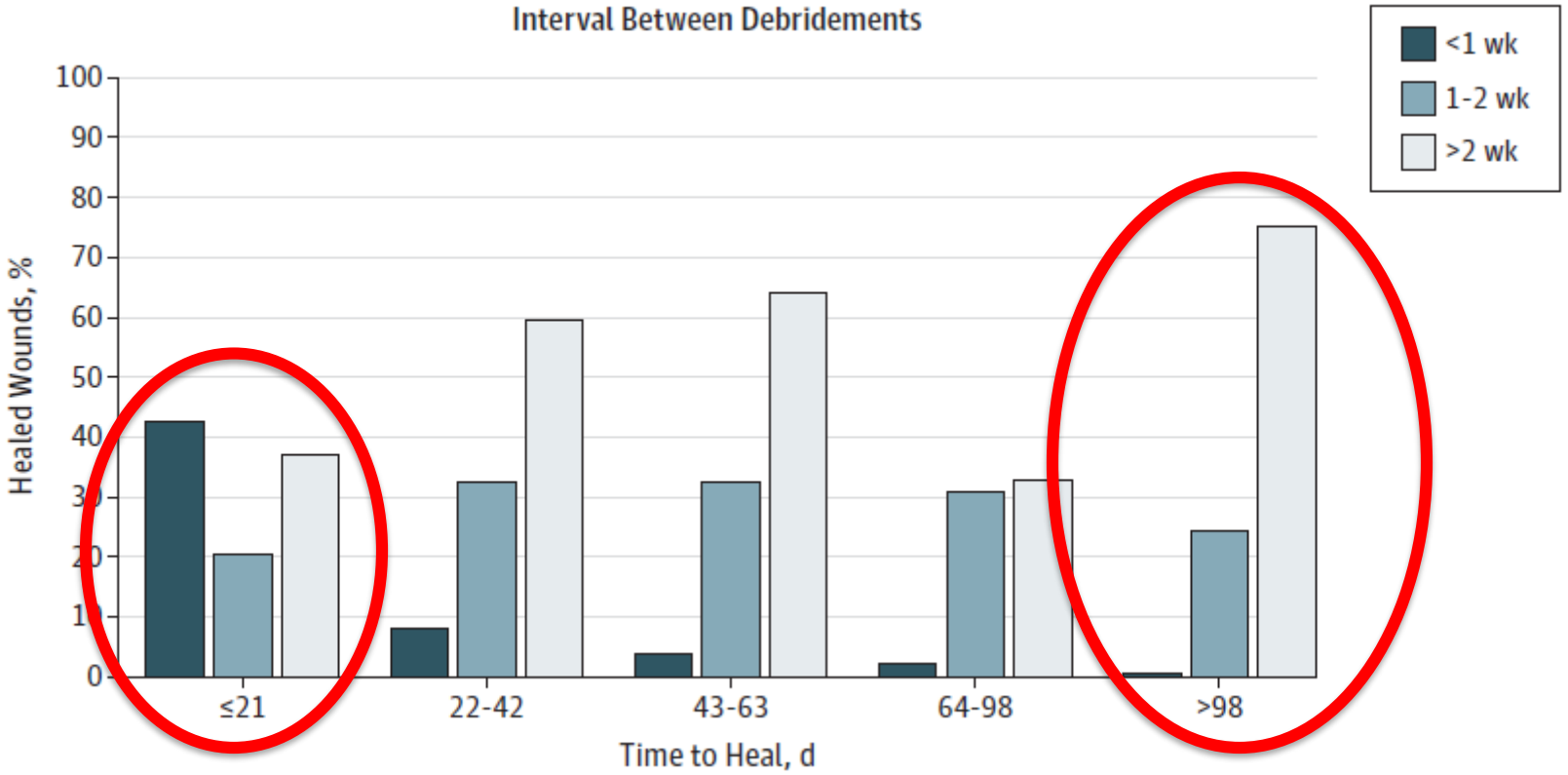
Debridement Frequency vs. Days to Heal: All Wound Types (321,744 Wounds)



Wounds with debridement intervals of 1 week or less healed significantly faster.

J Wilcox et al. JAMA Dermatology. 2013; 149 (9): 1050-1058.

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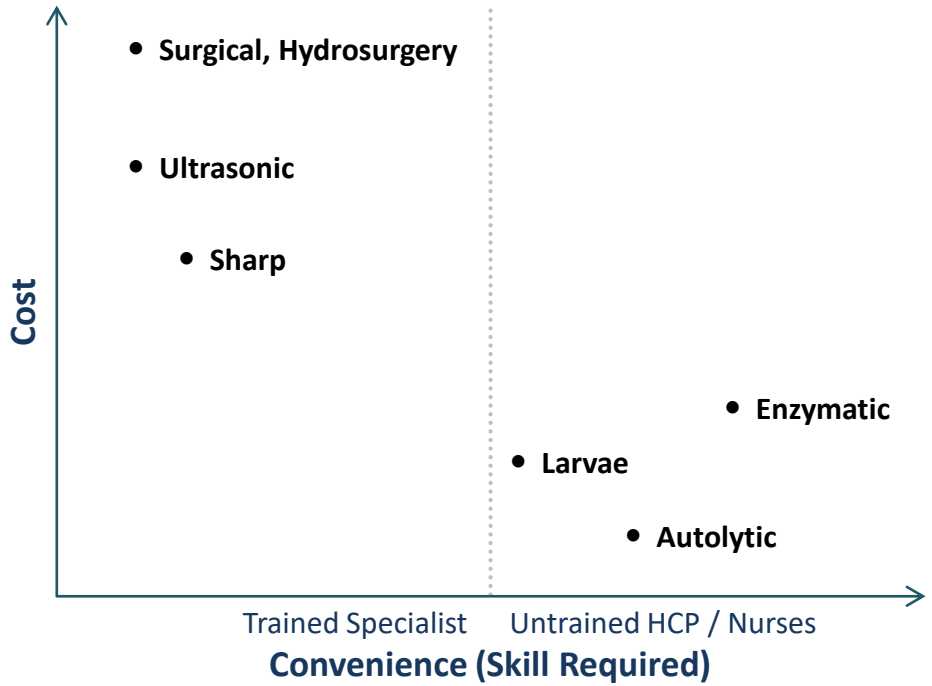
Types of Debridement

Strategy	Description	Examples
Surgical (Excisional/Sharp)	Removal by surgical instrument	Scalpel, scissors, hydrosurgery, lasers, curettes
Mechanical	Removal of necrotic tissue by mechanical means	Wet- to dry dressings, hydrotherapy, ultrasound, abrasion
Biosurgical	Sterile larvae selectively digest necrotic tissue and bacteria	Sterile blowfly or housefly larvae
Autolytic	Uses the body's own enzymes to dissolve necrotic tissue; assisted with moisture-retentive dressings	Moisture retentive dressings
Enzymatic	Topical application of enzymes to liquefy necrotic tissue	Collagenase

Weir D, Niezgoda J, Scarborough P. Wound Debridement, In: Krasner DL, Rodeheaver GT, Sibbald RG, eds. *Chronic Wound Care: A Clinical Source Book for Healthcare Professionals.* 4th edition. Malvern, Pa: HMP Communications, 2007: 343 – 355.

Current Standard Of Care



Factors to Consider

- Homogeneity
- Pain
- Bleeding
- Cost
- Setting
- Convenience

Significant Medical Need for Rapid and Effective Debriding in Outpatient Settings

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Opportunity

- The rapid non surgical – low skill level debriding agent
- Agent for skilled nursing facility patients
- Rapid wound bed prep prior to skin grafting
- Short duration focused therapy

Summary and Conclusion

- Debridement is the cornerstone of great wound care
- Selecting type of debridement is dependent on a number of factors
- Debridement is part of the planning process of advanced therapies

Market Landscape Analysis & EscharEx Market Potential

Ilina Sen, Life Sciences Senior Director
Huron Consulting Group

HURON

Market Research Has Been Comprehensive

Robust Qual / Quant Research

- In-depth interviews (N=30) with KOLs, community practitioners, payers in US / EU
  - Current & future treatment dynamics
  - Feedback on EscharEx profile and positioning
  - Pharmacoeconomic considerations
- Web survey (N=200) fielded to quantify the opportunity for modeling (e.g. eligibility rate, tx rate, shares, etc.)

Refreshed Qualitative Research

- In-depth interviews with VLU treaters (2020) across diverse specialties to reflect range of treaters that see VLU patients (N=10, 45 min each)
- Interviewees represented diverse geographic mix across the US
- Discussion focused on clinical and commercial topics of interest related to the evaluation of EsharEx potential

Market Sizing Analysis

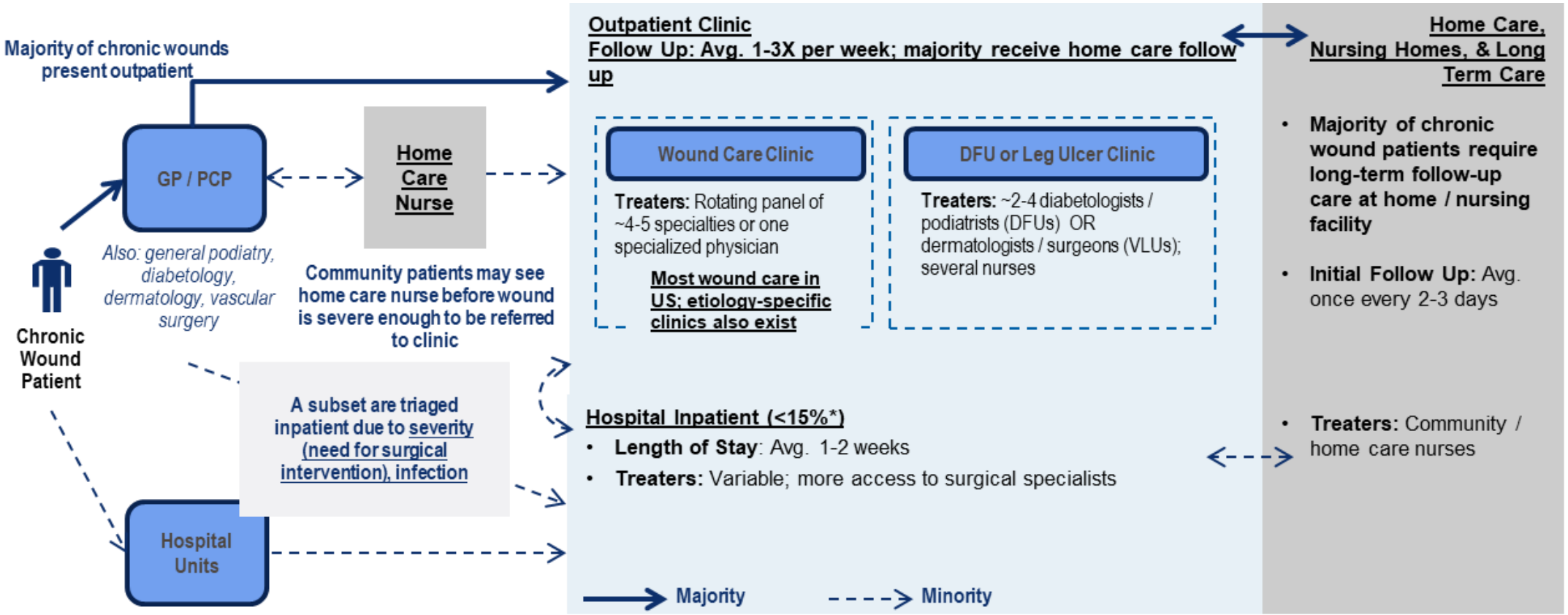
- Performed market sizing analysis for VLUs and DFUs
- Triangulated estimates across range of sources including literature, syndicated market research, and analyst reports
- Perform analog research to identify benchmarks to guide time to peak adoption estimates

Market Potential Evaluation

- Created a 10-year forecast for ExcharEx in VLUs and DFUs
- EshcarEx market share estimates were based on prior rounds of market research
- Output included VLU and DFU revenue estimates building to total EscharEx market potential

HURON

Chronic Wound Patient Journey: Key Site Care

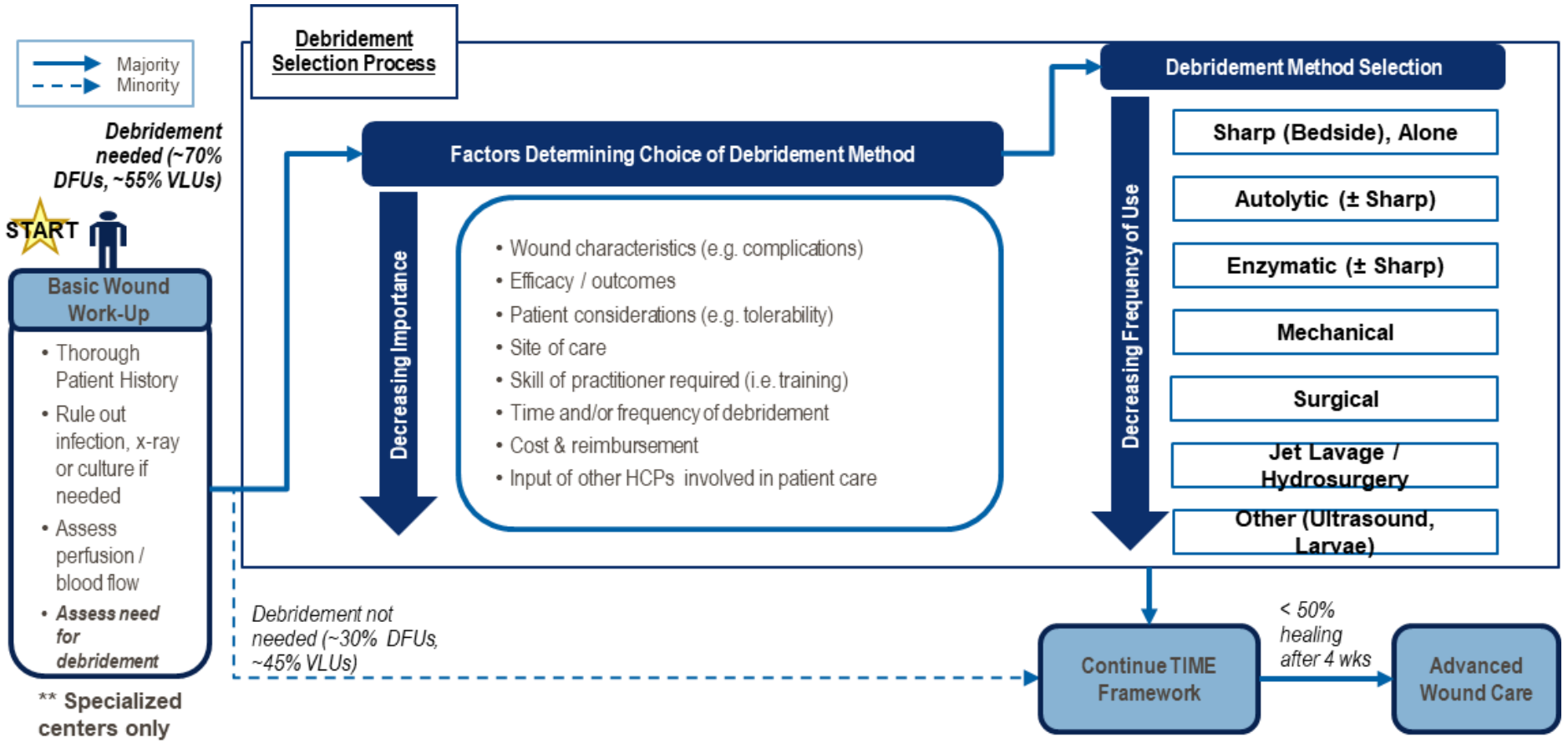


Most Chronic Wounds in The U.S. are Treated Outpatient with Follow-up Visits 1-3x per Week

HURON

* 15% present in academic setting w/ more complex wounds; overall % inpatient likely lower

Debridement is SOC, But Method is Not Standardized

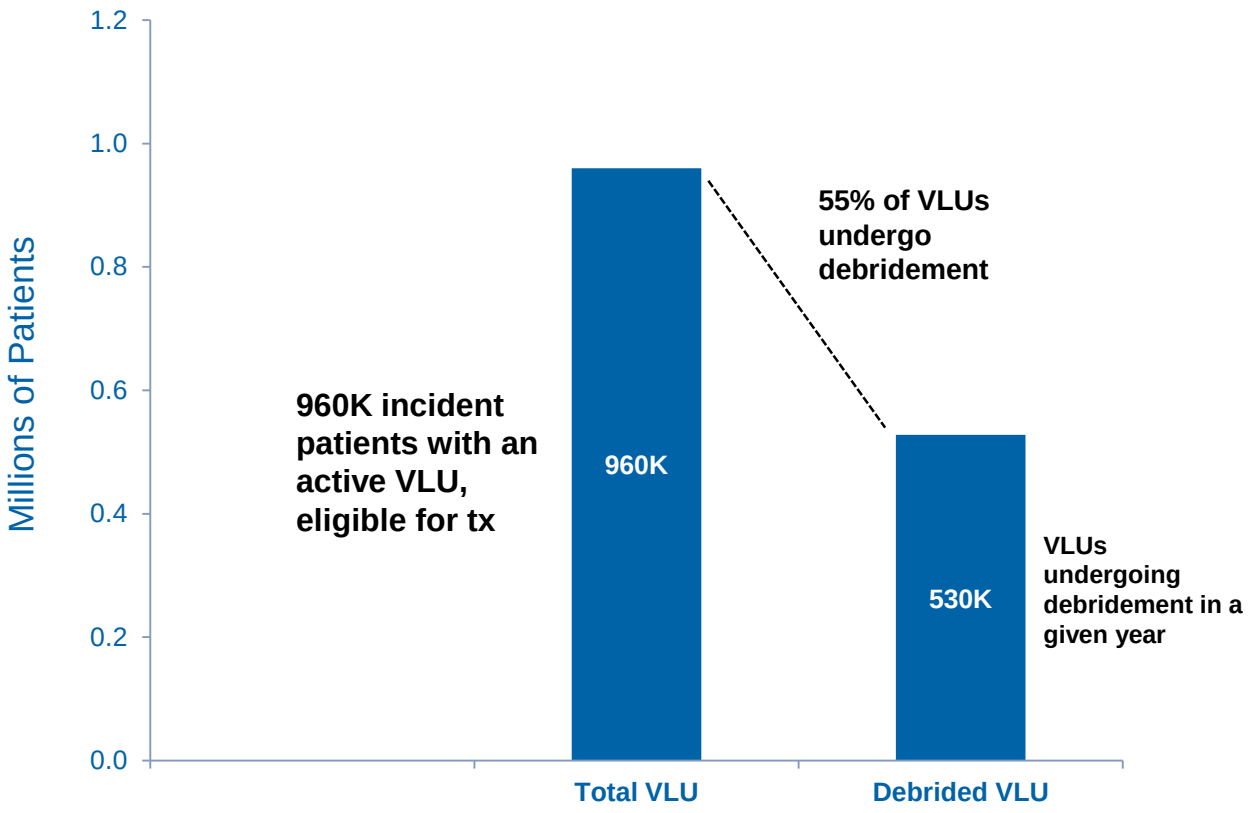


Wound characteristics, efficacy, and patient considerations are top influencers of choice

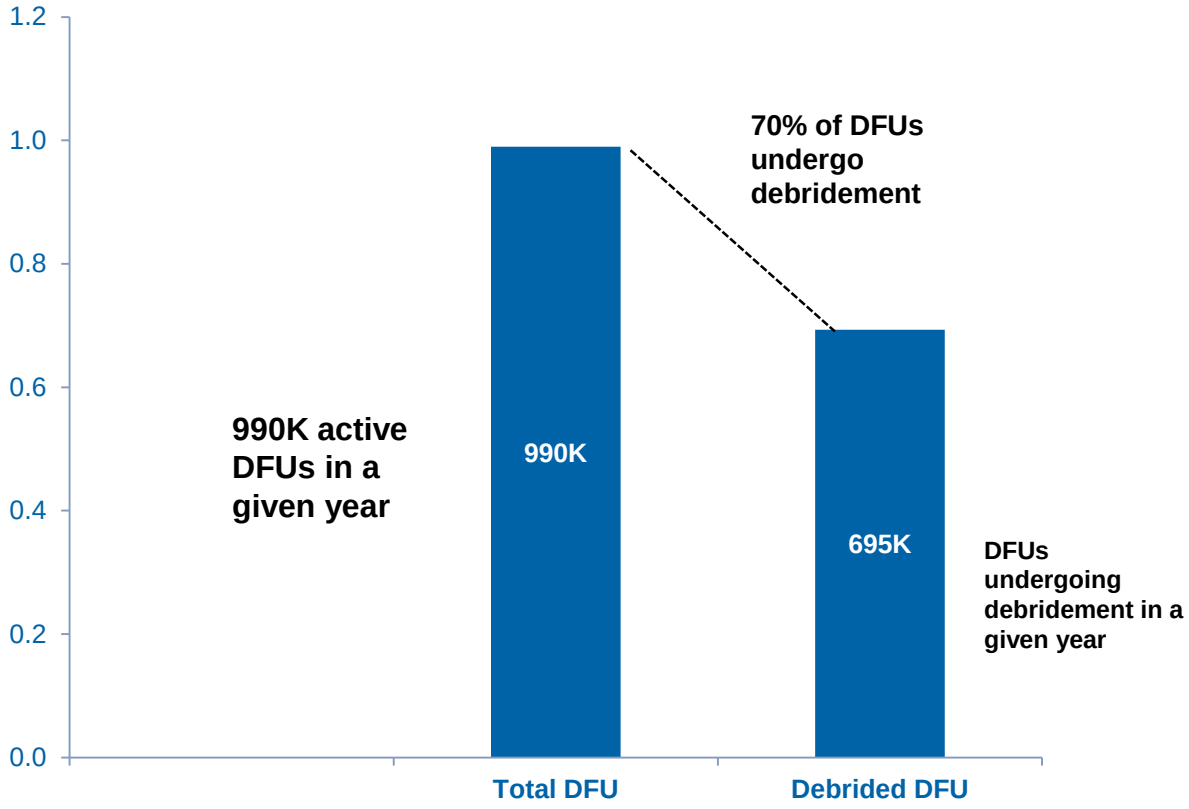
HURON

Triangulation Indicates ~960K VLUs and ~990K DFUs Annually Eligible for Debridement

2019 US VLU Epidemiology Estimate



2019 US DFU Epidemiology Estimate



HURON

Source: US Census Bureau, Huron Primary Research (2015)

VLU Debridement Approach Driven by Site of Care

Current Use of Debridement Approaches

Technique Type	%s of VLUs Debrided*	Drivers of Use	Treaters
Sharp (Only)	~40%	• Fastest method • High efficacy	• WC clinic (surgeons or other trained staff)
Enzymatic (Only)	~15%	• Can be applied in any setting • For patients who do not want to undergo sharp	• Practices less suitable for sharp (e.g. other specialty practice, nursing home)
Sharp + Enzymatic	~10%	• For patients with fibrotic tissue in wound after sharp	• WC clinic (surgeons or other trained staff)
Autolytic (Only)	~15%	• Can be applied in any setting • Most affordable, used for less severe wounds	• Home health, nursing homes
Sharp + Autolytic	~10%	• For patients who need continued debridement after sharp	• WC clinic (surgeons or other trained staff)
Other (including other combo of sharp & ultrasound, hydrotherapy, etc.)	<10%	• Ultrasound helpful in patients with high pain, but equipment / biological agents not available at many practices	• Limited number of more comprehensive WC clinics

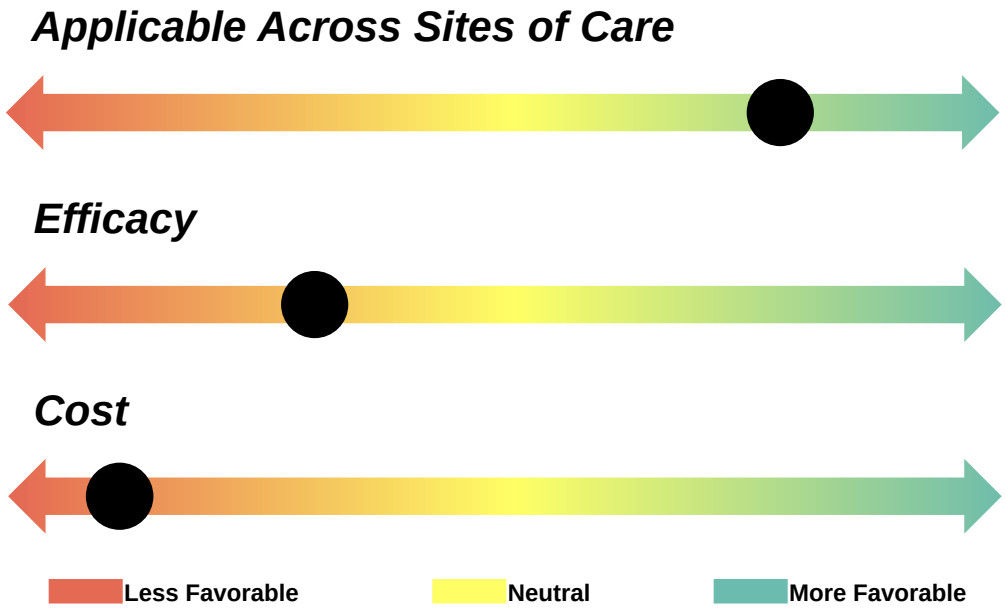
*Estimates are based on small study (N=10)

Commentary

- **All VLU patients seen at WC clinics will undergo debridement**
  - In contrast, in home health setting only 1/3 VLUs are debrided
  - Other 2/3 of patients have wounds that are caught and managed early by nurses, and thus can heal without needing debridement
- **Choice of debridement technique is highly dependent on site of care**
  - Surgeons and clinicians at wound care clinics, regardless of medical specialty, **perform sharp debridement as SOC for all patients**
  - In other specialty practices, such as dermatology, **clinicians much more split between sharp vs. non-sharp**
  - As expected, nursing home / home health settings depend enzymatic or autolytic and will refer patients to WC clinic if severe

Current Enzymatic Use is Limited, Due to Perception of Low Efficacy and High Cost

Current Enzymatic SOC Perception



Commentary

- **Sites of Care / Use Case:** Use restricted as adjunctive in settings where sharp is preferred (surgery or WC clinics), with greater use in sites where sharp is less accessible (nursing homes, and home health)
- **Efficacy:** Opinion of enzymatic efficacy ranges very low to moderate
  - Application is almost always less frequent than daily (daily only possible in nursing homes and for patients with caregivers; 2-3 days more common)
  - Efficacy is modest, and can be impacted when used with other topicals
  - While time to debridement with enzymatic standard of care varies based on wound size, duration, with average use of ~6-8 weeks
- **Cost**: High cost cited as major disadvantage of enzymatic
  - 2019 AWP $284 / 30g; reimbursed under pharmacy benefit
  - Prior research showed patients used ~6-8 tubes on avg (total ~$2000 AWP)

HURON

Source: Huron Primary Research (12/2019)

There Exists Significant Need for Rapid-Acting and Safe Enzymatic Agent, Filling Gap Left by Panafil/Accuzyme

Unmet Need

- Clinicians voice the **need for an effective, safe, and affordable non-surgical debridement agent,** as sharp is not suitable for all sites of care and require trained staff to perform
  - Ideally this product will require less frequent application than enzymatic debridement approaches and causes low pain
  - **Gap in market remains after recall of papain products** (seen to be much more effective than enzymatic standard of care), which were used commonly in sites of care not suitable for sharp procedures
- Outside of new product needs, logistics and adherence challenge exist with patient getting to clinics, timely change of dressing, elevating leg, etc.

Pipeline

- KOLs note awareness of **crowded pipeline for chronic wound care healing products**
- **Pipeline is limited for debridement products**

"*There is an **enormous unmet need for an enzymatic debridement agent that is more rapid acting and safe**.*
…Accuzyme was a hundred-million-dollar drug and rightfully so, it really was a very good. I used a lot of it and I was a lot more likely to use it after my sharp debridement than enzymatic. So I think there is a huge unmet need. "

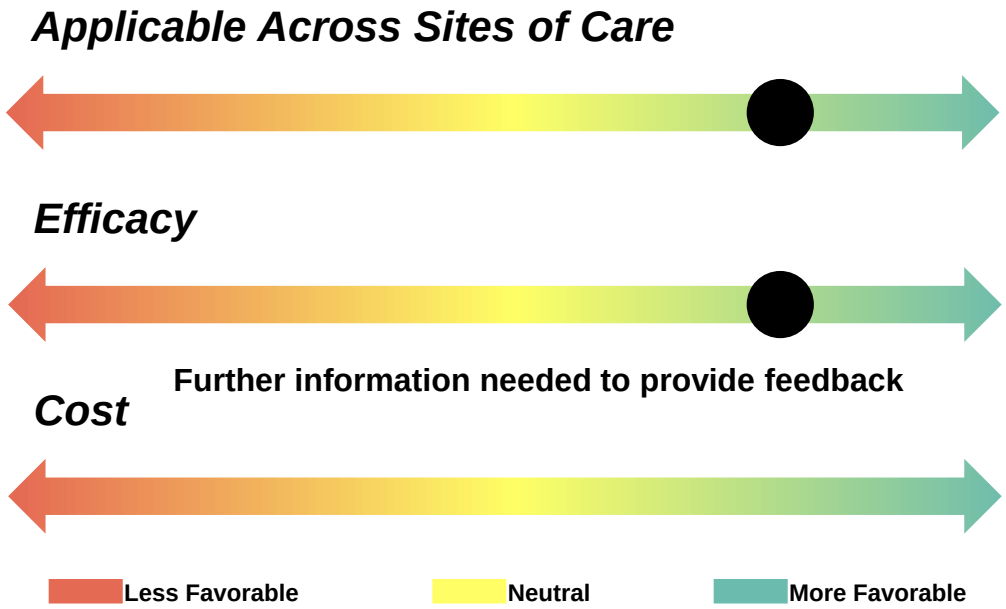
- US KOL #2

HURON

Source: Huron Primary Research (12/2019)

Given Significant Unmet Need, EscharEx Welcomed as Another Option, Especially for HCPs Relying on Non-Sharp

EscharEx Perception By Product Attribute



Commentary

- **Eligible Patient Population (similar to current enzymatic):**
  - Patients seen at sites of care not conducive for sharp
  - As adjunctive to sharp in WC clinic settings
  - Patients not suitable for sharp (anxious, sensitive to pain, or have arterial disease)
  - Patients with removable compression to enable frequent application
- **Efficacy:** Feedback was most positive in specialties with lower sharp use (e.g. nurses, dermatologists); for sharp treaters, H2H vs. current enzymatic standard of care is important to drive EscharEx adoption with superiority data seen as clinically meaningful
- **Application:** Daily dosing noted as challenging, but not a disadvantage compared to current enzymatic treatment

HURON

Source: Huron Primary Research (12/2019)

U.S. Market Opportunity

~2,000K
VLUs & DFUs patients eligible for debridement in a given year

55%-70%
Percentage of wounds debrided

32%
Percentage debrided by enzymatic methods
(Research indicates that EscharEx can expand enzymatic market (20% today) if superior to current enzymatic agent and more cost effective)

70%
Anticipated EscharEx market share based on superiority
5 Years-to-Peak Share

CoT: $1,500 (base) / $1,800 (upside) / $1,200 (downside)
CoT: based on 5 applications on average @ $300 per application

- **EscharEx TAM for VLUs and DFUs is estimated at $2B in the U.S.**
- **EscharEx potential market share is estimated at 20%-25%**

HURON

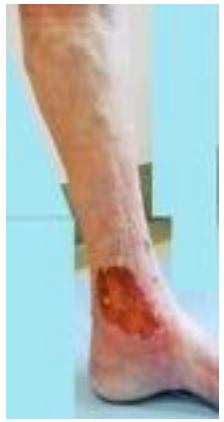
Market potential estimates based on above assumptions, and does not account for market access and other considerations that may impact actual figures and are subject to EscharEx approval by FDA . EscharEx is an investigational Drug under development, not approved in any jurisdiction

Stony Brook Medicine

Development of a Porcine Model for Eschars and Evaluation of a novel Bromelain-Based Enzymatic Debriding Agent

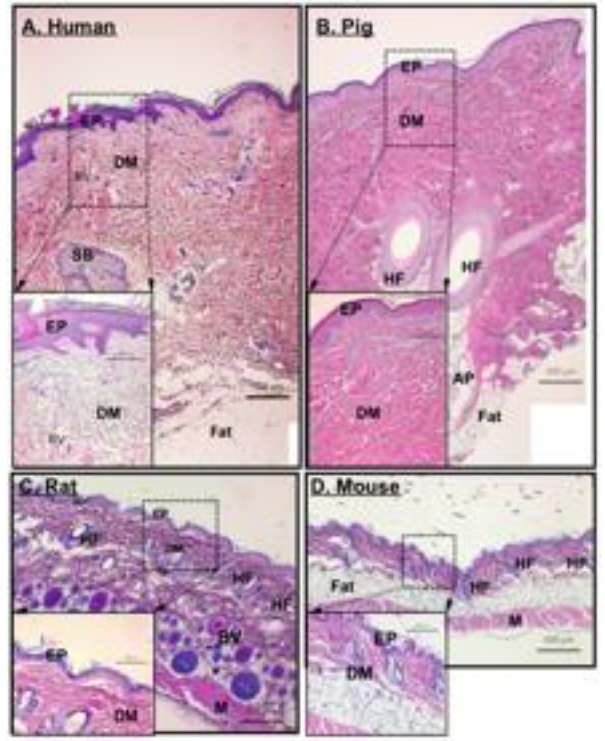
Adam J Singer, MD; Itai Sabbag, DMV; Yaron Shoham, MD

Department of Emergency Medicine
Renaissance School of Medicine at Stony Brook University
Stony Brook, NY



Stony Brook Medicine

- Over 6 million chronic wounds annually
- Development of novel therapies limited by lack of animal models
- Pigs are optimal animal model for wounds
- Doxorubicin known to cause skin necrosis after accidental extravasation



Background

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- Develop a novel porcine eschar model using intradermal injection of doxorubicin
- Assess the efficacy of a novel bromelain-based enzymatic debridement agent in this model
- Compare the efficacy of a bromelain-based enzymatic debridement agent with a commercially available enzymatic debridement agent

Study Objectives

- Full thickness excisional wounds created on 3 pigs
- Wound edges injected with various concentrations (0.25, 0.5, 0.75 mg/ml) and volumes (2.4, 4.8 ml) of doxorubicin
  - Thin layer of petrolatum gauze for 9 days
  - Non-permeable layer of parafilm days 9-10
  - Dry gauze days 11-20
- Wounds monitored for a period of 46 days for the development of eschar

Methods

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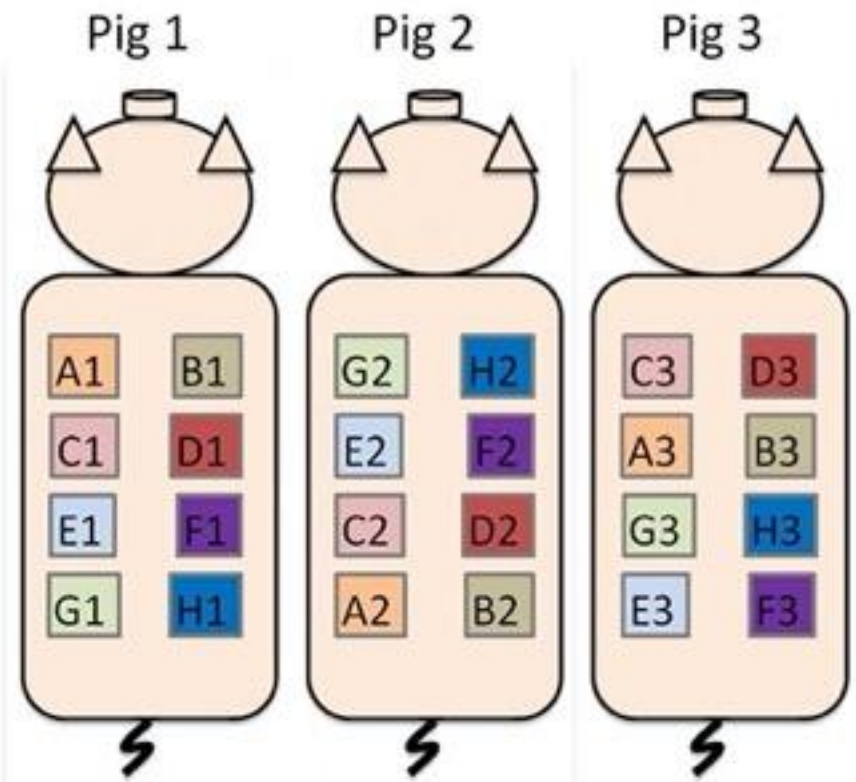

A (1,2,3): Control, untreated wound
B (1,2,3): Control, untreated wound
C (1,2,3): 0.25mg/ml Doxor ml.
D (1,2,3): 0.25mg/ml Doxorubicin 4.8 ml.
E (1,2,3): 0.5mg/ml Doxorubicin 2.4 ml.
F (1,2,3): 0.5mg/ml Doxorubicin 4.8 ml
G (1,2,3): 0.75mg/ml Doxorubicin 2.4 ml.
H (1,2,3): 0.75mg/ml Doxorubicin 4.8 ml.

Experimental Design

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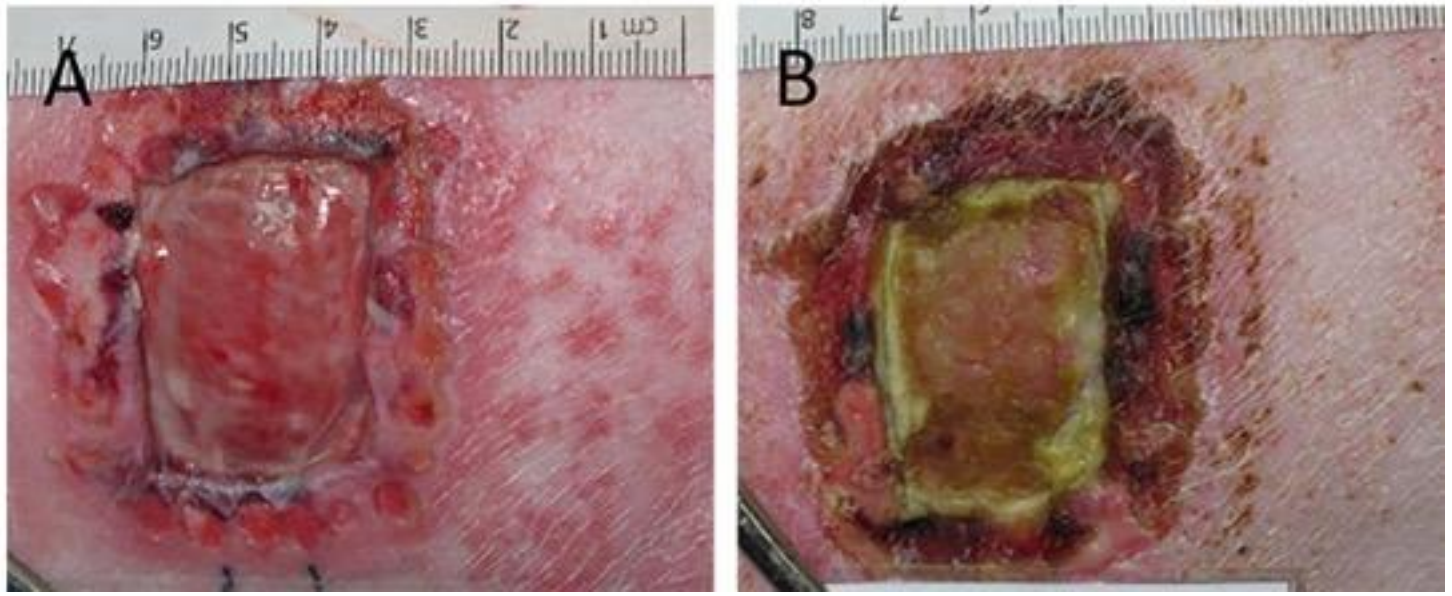
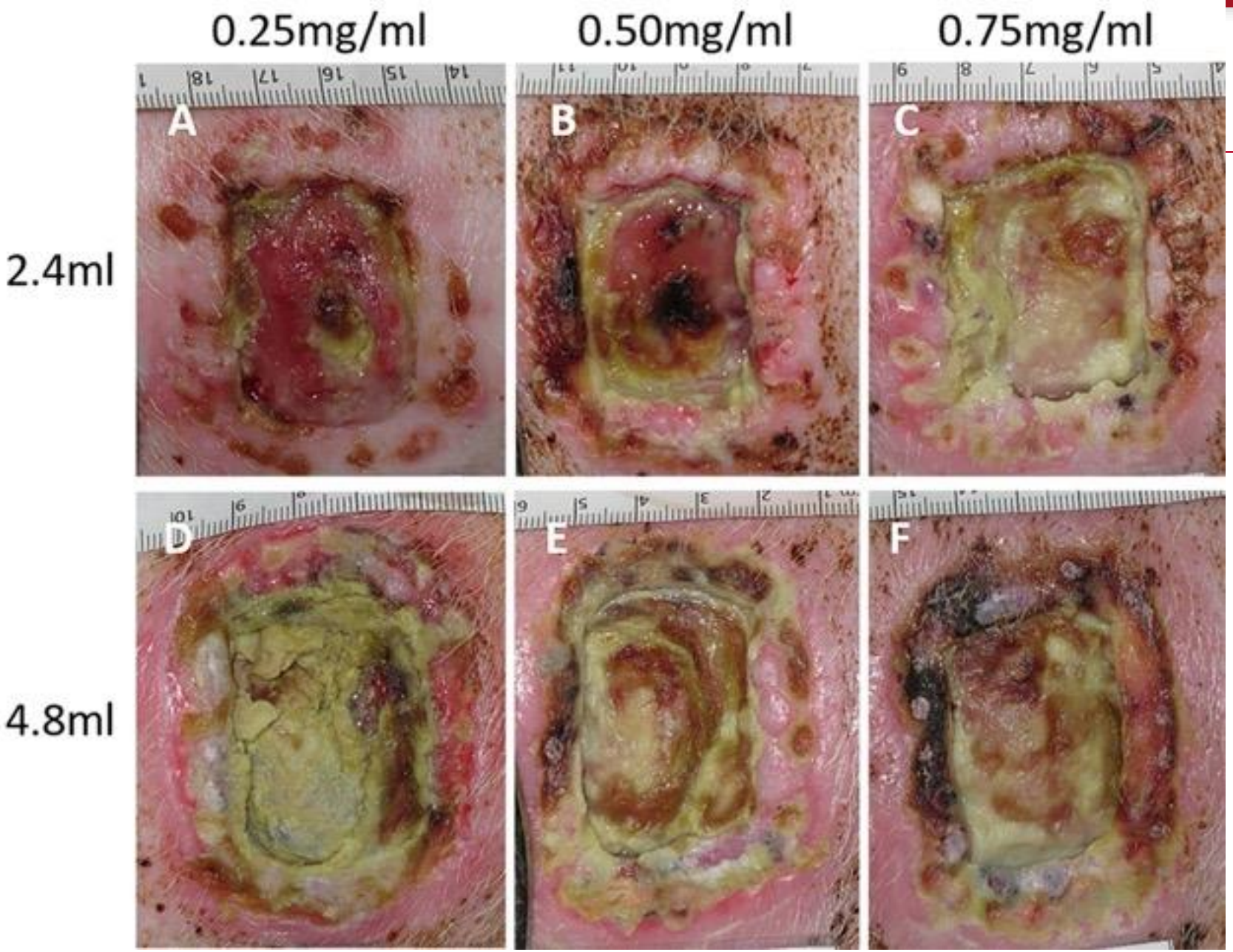


A) a full-thickness excisional wound 10 days post infliction, covered by occlusive dressing. Erythema in the healthy skin surrounding the wound is distinct.
B) A wound 18 days post infliction, covered by gauze. Two distinct eschar types are apparent. In the center, a slough composed of materials secreted from the wound, and in the periphery, completely necrotic skin where doxorubicin was injected. The healthy skin surrounding the wound (peri-wound) shows no apparent irritation.

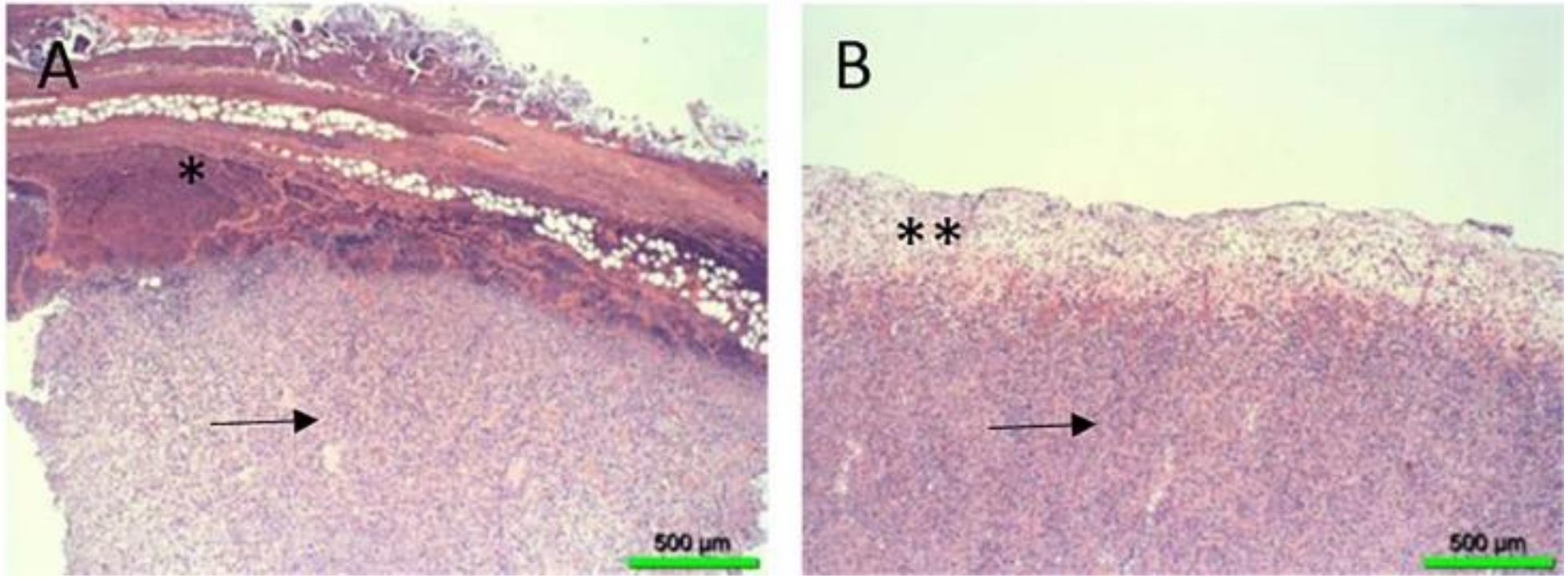
Model Development



Representative 3 cm × 3 cm chronic wounds with varying concentrations and volumes of doxorubicin injection. With increasing volumes and concentrations, the necrotic tissue at the wound periphery is more homogenously dispersed and the central eschars is thicker.

Model Development

Stony Brook Medicine



A) A representative micrograph of H&E-stained tissue taken from the wound. A. Wound periphery. Mummified skin including deep dermis and underlying fat. * Infiltrate rich in inflammatory cells. Arrow denotes deep granulation tissue.
B) Wound center. ** Edematous granulation tissue. Arrow denotes deep granulation tissue.

Micrographs Of Experimental Wounds

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- Additional wounds created on another set of animals
- Eschars treated with up to 16 daily applications of various concentrations (0.1%, 0.5%, 1%, 2%, 5%) of EscharEx or commercial collagenase debridement agent
- EscharEx: concentrate of proteolytic enzymes enriched in bromelain derived from pineapple stems

Methods: Assessment of Wound Debridement

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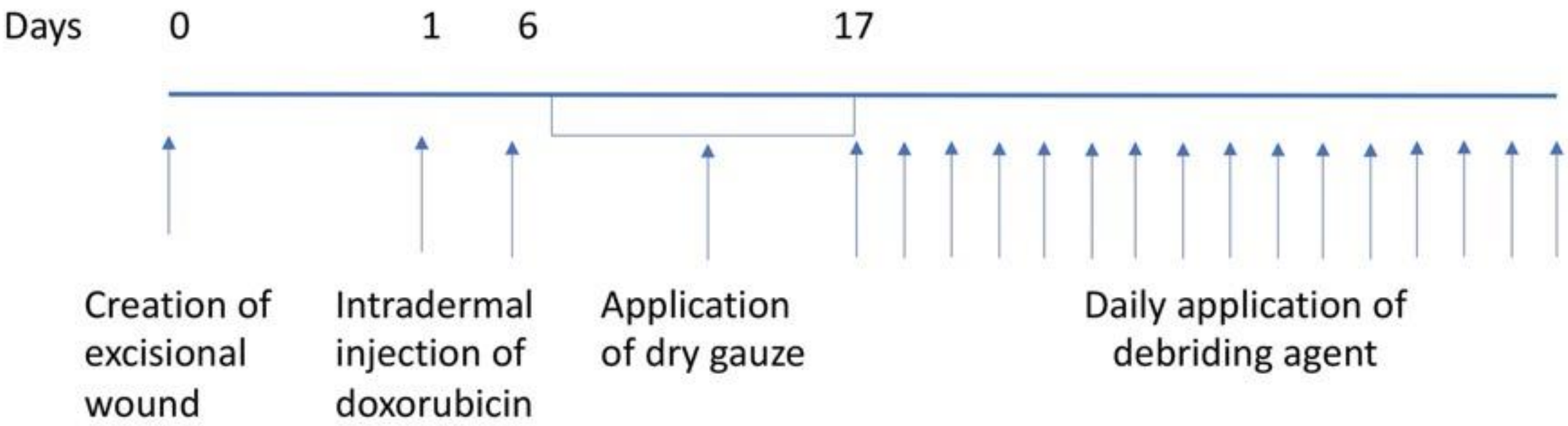

Schematic of Study Design

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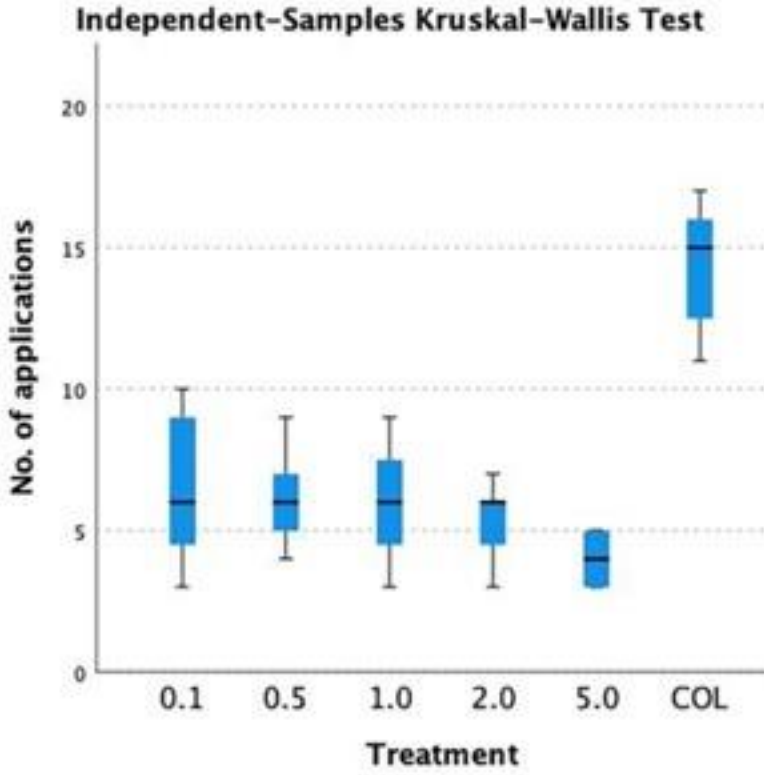

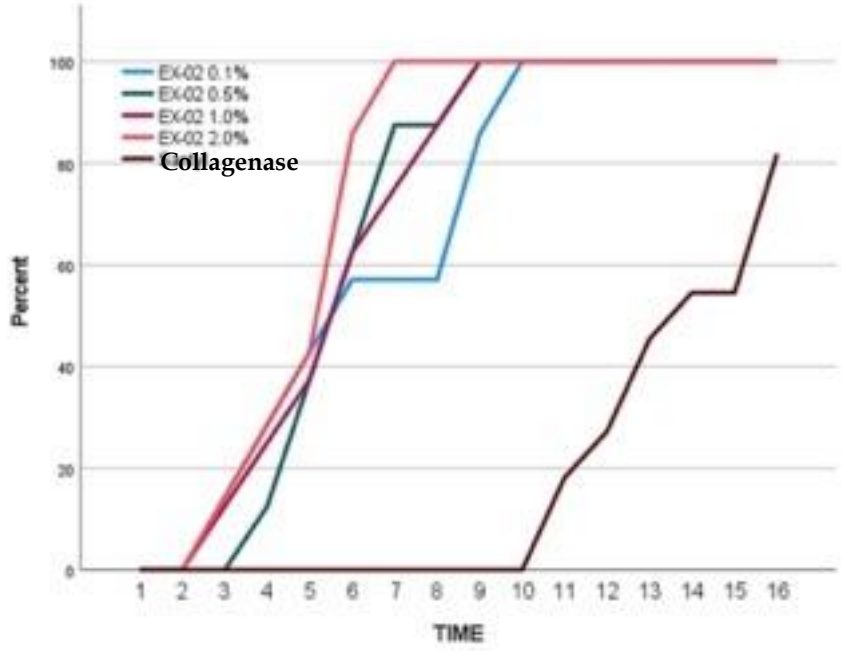

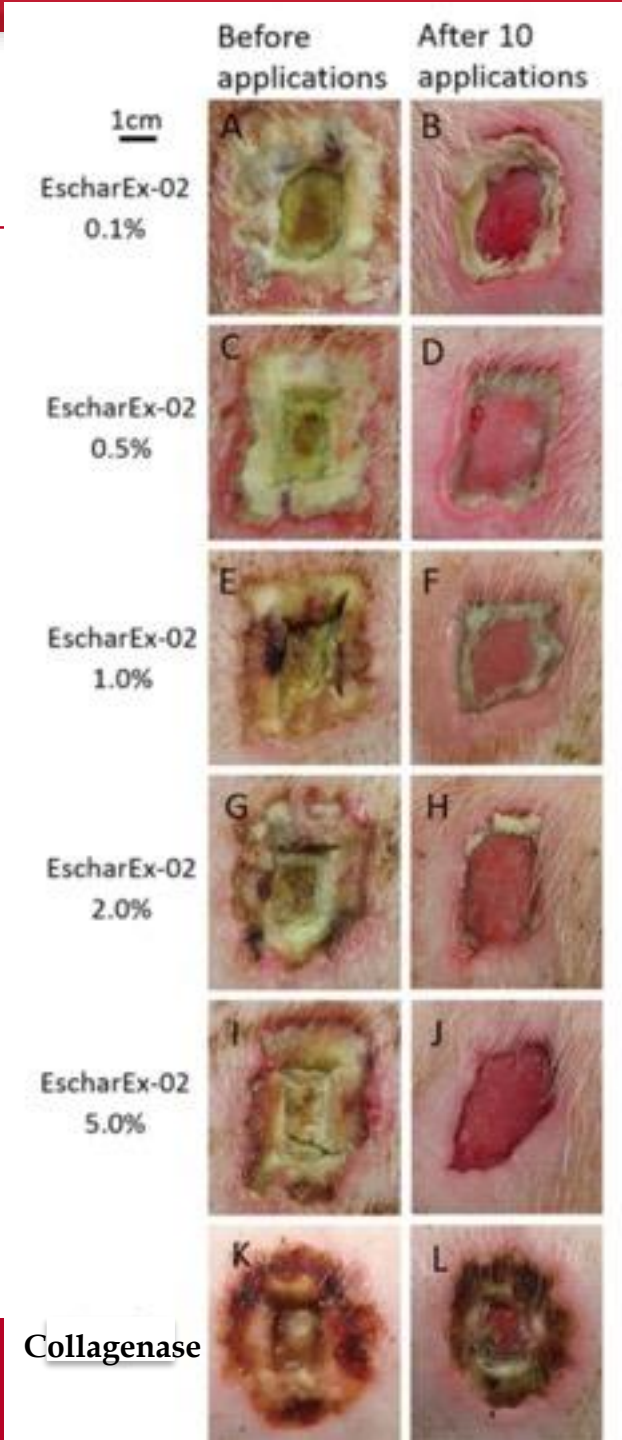

Dose Response Efficacy

- Central eschar seen in human chronic hard to heal wounds consistently formed in pigs by intradermal injection of doxorubicin
- EscharEx is more effective than commercial collagenase debridement agent in debriding eschars
- Consistent with prior study of contaminated ischemic porcine wound model

Summary of Study Results

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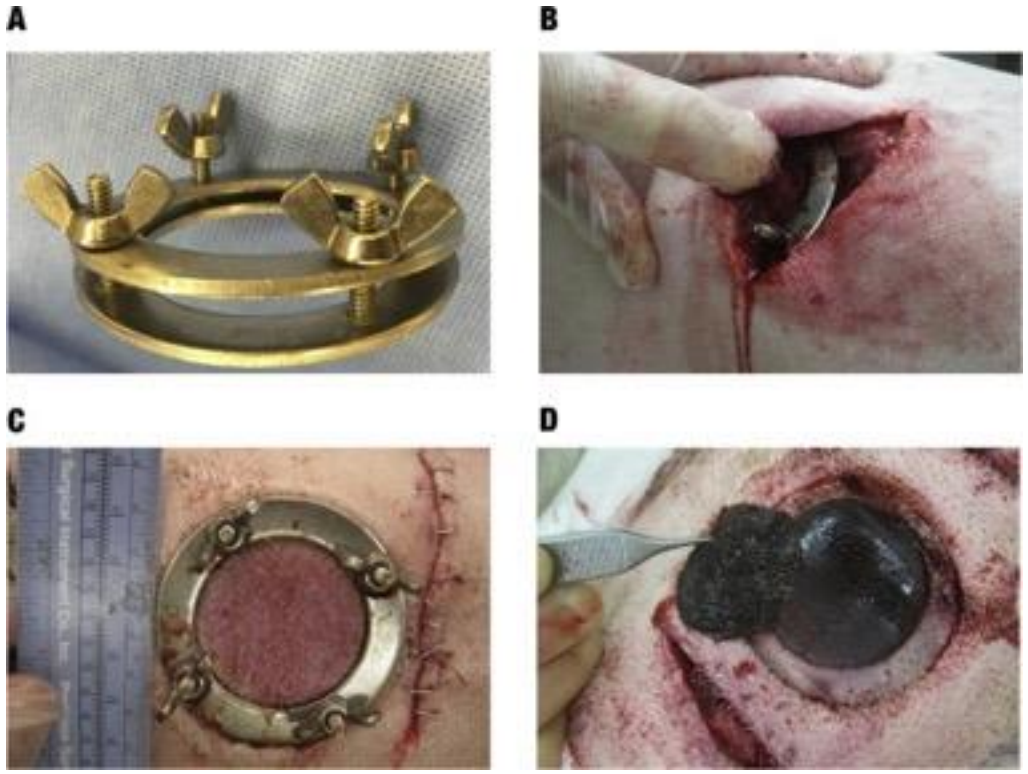
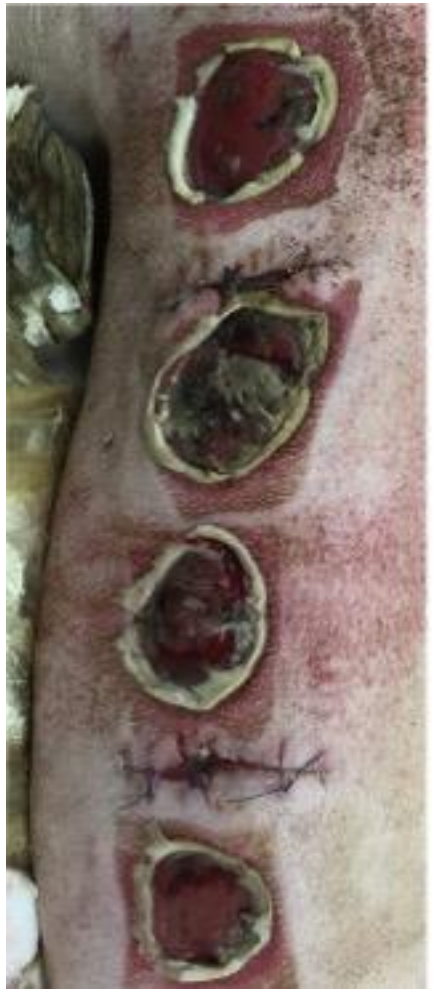
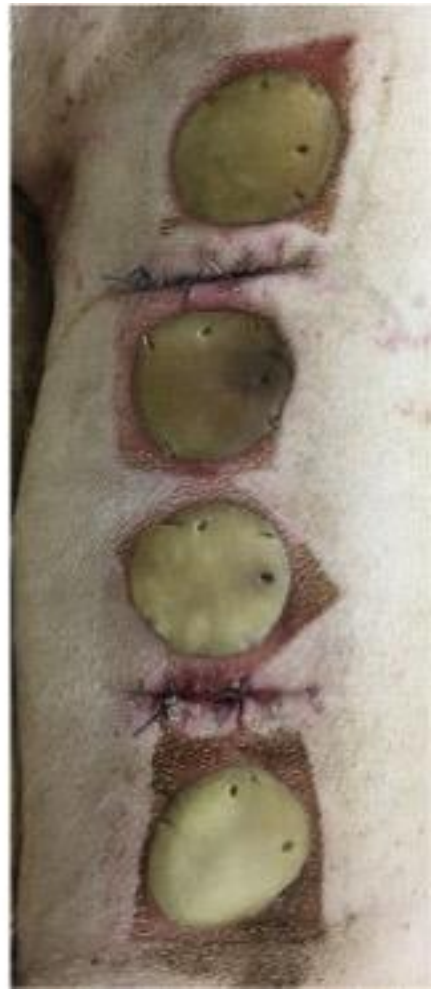
Singer et al. Burns 2018;44:896



EscharEx



Vehicle



Development of a contaminated ischemic porcine wound model and the evaluation of bromelain based enzymatic debridement

- Small sample size
- Pigs vs. humans
- Short term follow-up

Limitations

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- We describe a porcine model for creating eschars similar to chronic wounds in humans
- A novel bromelain-based enzymatic debridement agent was significantly more effective than a commercially available collagenase in removing eschars in this wound model
- These data support ongoing clinical trials of EscharEx

Conclusions

EscharEX

A '*Triple Threat*': Managing Biofilm/ Bioburden

Robert J. Snyder, DPM, MSc, MBA, CWSP

Chief Medical Director, Mediwound

Interim Dean, Professor and Director of Clinical Research

Barry University School of Podiatric Medicine

Dr. Robert Snyder

- Chief Medical Director, Mediwound
- Interim Dean, Professor and Director of Clinical Research, Barry University School of Podiatric Medicine
- Practice limited to wound management and limb preservation for more than 30 years
- Principal or Lead Investigator on more than 65 randomized controlled trials
- Published more than 165 peer-reviewed and trade journal articles on wound management and related topics
- Lecture nationally and internationally on wound management

Objectives

- Discuss an overview of managing biofilm/bioburden in chronic wounds
- Review bromelain and its effect on biofilm
- Learn about the new pharmacology study regarding EscharEX
- Describe why EscharEX may be a ‘Triple-Threat’ to chronic wounds

What is the Problem

- ”Microbial infections are the single most important cause of chronic, non-healing wounds. Chronic wound infections typically form biofilms, which are notoriously recalcitrant to conventional antibiotics..”. (Kadam et al 2019)

- “Bacterial biofilms are an ever-growing concern for public health, featuring both inherited genetic resistance and a conferred innate tolerance to traditional antibiotic therapies...” (LuTheryn et al 2019)

•

Kadam et al (2019)Biomedicines, *7*(2), 35

LuTheryn et al (2019)Microbial Biotechnology, *13*(3), 613–628

Infection Complicates the Treatment of Wounds and Impedes the Healing Process by:

- Damaging tissue[1]
- Reducing wound tensile strength[1]
- Inducing an undesirable inflammatory response[2]

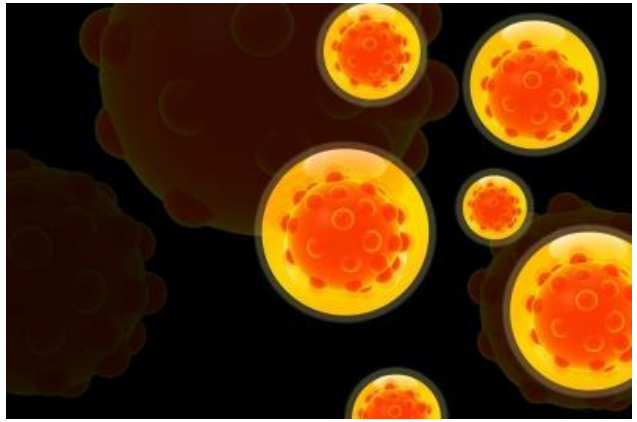


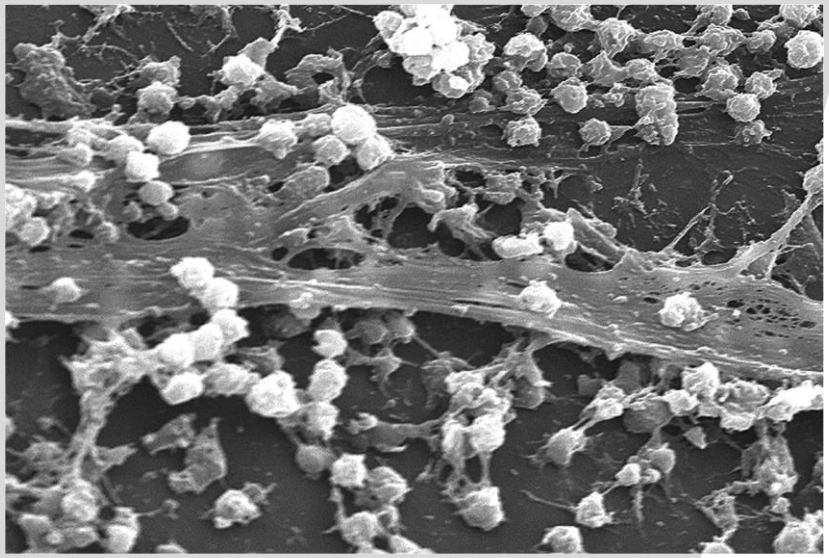
Image courtesy of renjith krishnan/ FreeDigitalPhotos.net

- **Thus, controlling or preventing infection is essential in order for the healing process to progress normally**

1. Wright JB Hansen DL, Burrell RE. The comparative efficacy of two antimicrobial barrier dressings: In vitro examination of two controlled release of silver dressings. *Wounds 1998; 10(6): 179-188.*
2. Yin HQ, Langford R, Burrell RE. Comparative evaluation of the antimicrobial activity of Acticoat** antimicrobial barrier dressing. J Burn Care Rehabil 1999; 20: 195-200.

What is biofilm?

Biofilm is a **community of pathogens** enveloped within a complex structure of **entangled polymers** strengthened with **metallic bonds**



Source image: https://phil.cdc.gov/Details.aspx?pid=7488

Image courtesy of CDC/Rodney M. Dolan, PhD. and Janice Haney Carr

Community of pathogens

Multiple species of bacteria and fungi living together.

Entangled polymers

Microbes secrete a protective matrix called EPS (extracellular polymeric substance) made from polymers including proteins, glycolipids, polysaccharides and DNA.

Metallic bonds

Metallic ions bind polymers of the EPS together forming a resilient-barrier.

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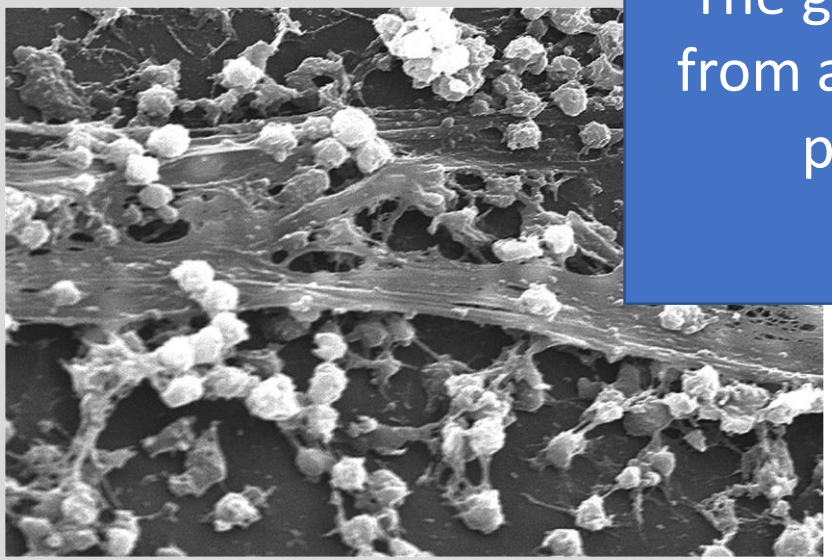

Source image: https://phil.cdc.gov/Details.aspx?pid=7488

Image courtesy of CDC/Rodney M. Dolan, PhD. and Janice Haney Carr

The glycocalyx protects the bacteria from antibiotics and accounts for the persistence of the infection

Community of pathogens

Multiple species of bacteria and fungi living together.

matrix called EPS
ance) made from polymers
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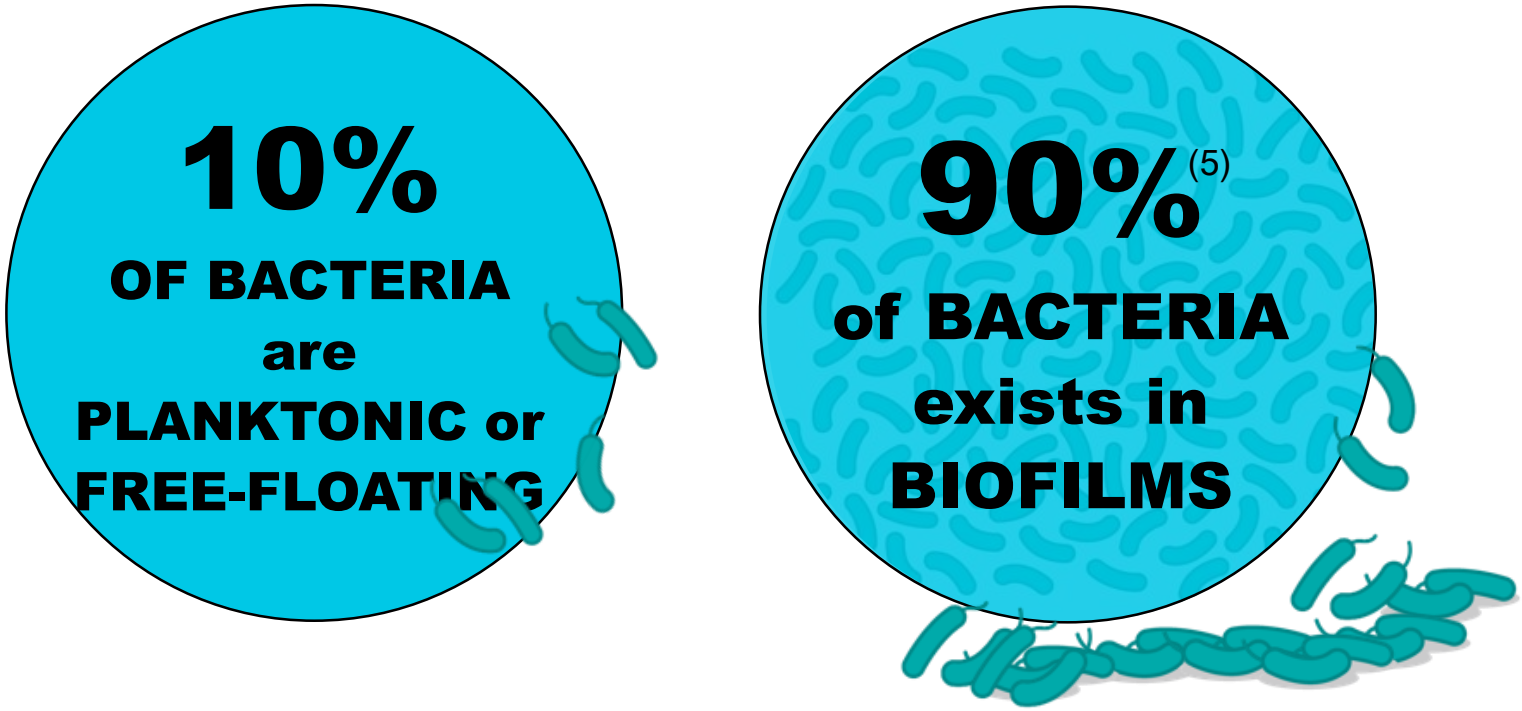
Most bacteria exist within biofilms

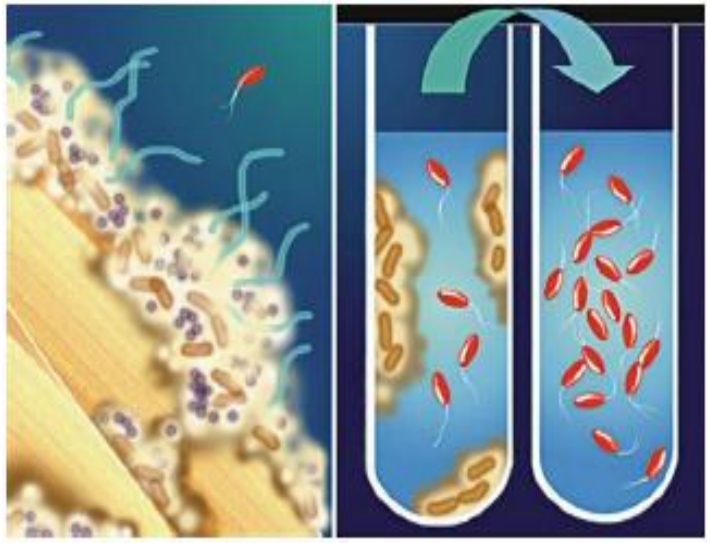


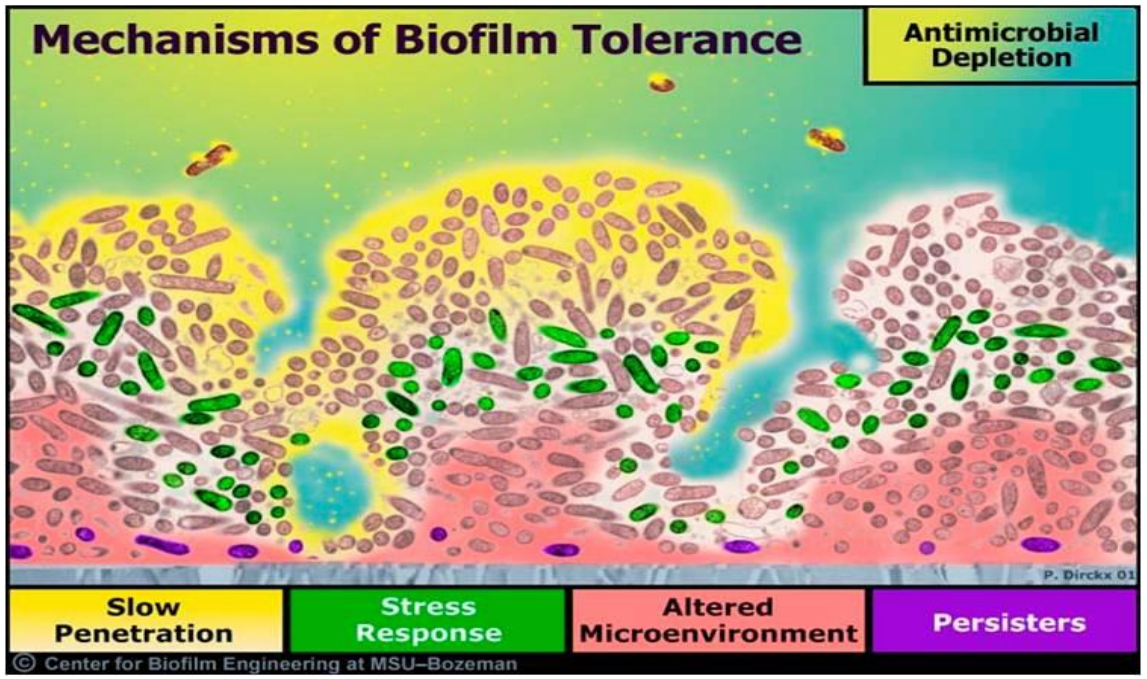
Bacteria protected by biofilm EPS (extracellular polymeric substance) can be **1000x more tolerant** to antibiotics than planktonic bacteria.

Snyder RJ et al (2017)
Wounds, 29(6 supp): S1-S1

Biofilms Don’t Play Fair

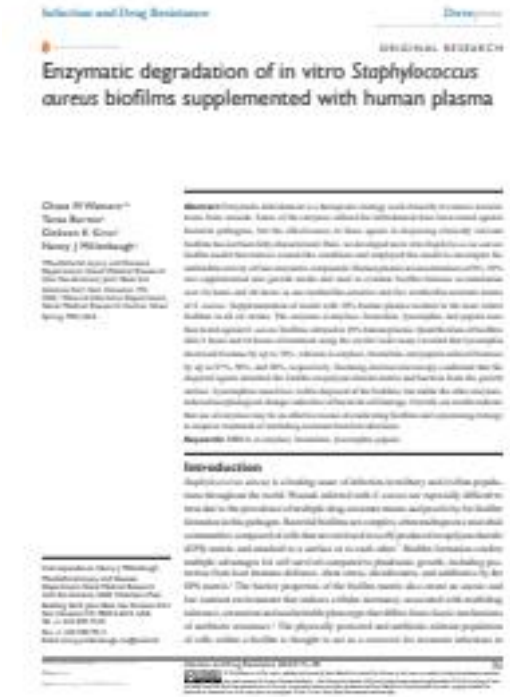
- Difficult to culture
- Tolerant of biocides
- Tolerant of antibiotics
- Capable of regenerating





Biofilm phenotype highly adapted for survival in the harshest of environments

The Benefits of Bromelain



Enzymatic degradation of in vitro *Staphylococcus aureus* biofilms supplemented with human plasma

- Staphylococcus aureus biofilm model that mimicked wound like conditions
- The antibiofilm activity of four enzyme compounds reviewed
- **Bromelain reduced biofilm mass by 98%**
- Scanning electron microscopy confirmed detachment of the biofilm EPS and bacteria from growth surfaces
- Overall, results indicated that enzymes such as **Bromelain** may be an effective means of eradicating biofilms and a promising strategy to improve treatment of multidrug-resistant bacterial infections

Clinical Pharmacology Study:

A prospective study performed to evaluate the clinical performance and pharmacology effect of EscharEx (EX-02 formulation) in debridement of lower leg ulcers (VLU and DFU): Clinical Phase II

Protocol Design

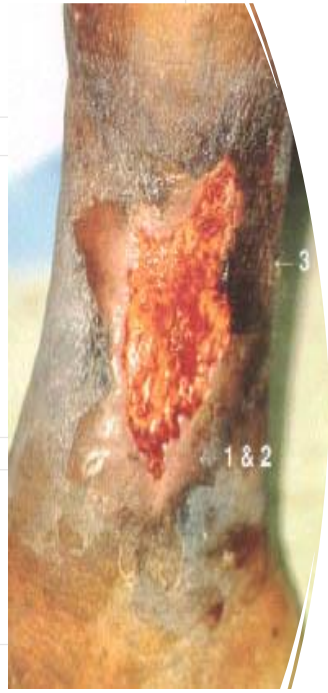
- Study objective - to test the pharmacological effect of EX-02 5% in patients with VLU and DFU
- Single arm, open label study
- Up to 15 patients, 2-3 US sites
- Duration – up to 8 treatment applications + 2 weeks follow-up
- Punch biopsies and wound fluids will be taken before and after complete debridement
- Evaluation with Moleculight

Data Collection

- Clinical performance- Incidence & time to complete debridement
- Effect on biofilm, bio-markers (i.e.: cytokines, MMPs) and planktonic bacteria
- Safety- systemic & local AEs, labs

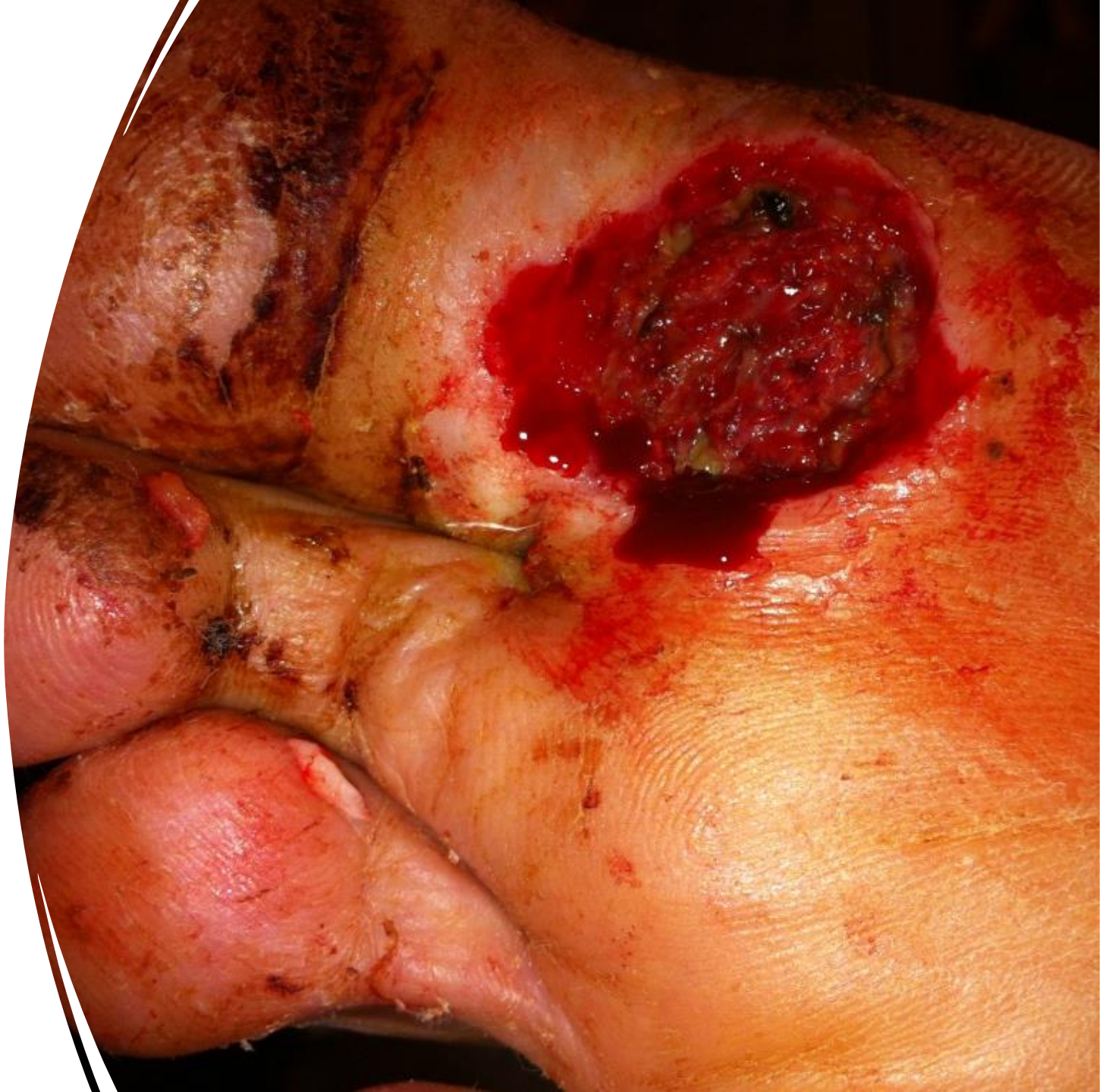
Timeline

- Study initiation is anticipated soon
- Data is expected by year-end 2021



EscharEX as a ‘Triple Threat’

- Efficient wound debridement may convert a chronic wound into one that is acute
- Bromelain could disrupt biofilm bacteria
- Bromelain could decrease planktonic bacteria

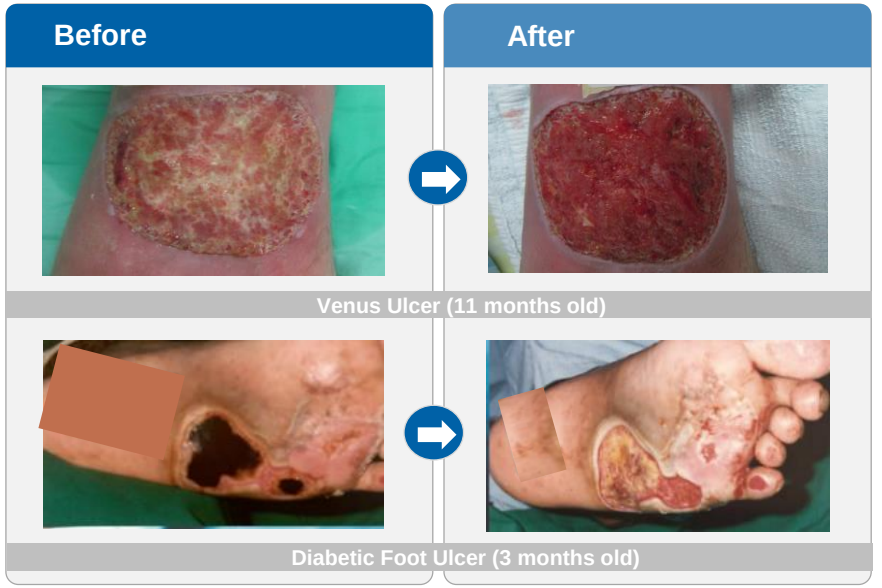


MediWound

EschaEx CDP and Business Update

EscharEx - Enzymatic Debridement for Chronic Wounds

- Investigational biological drug containing a mixture of proteolytic enzymes
- Designed for outpatient setting
- Inline with current treatment workflows and reimbursement landscape
- Easy to use, high potency for once a day topical application
- Designed to debride chronic wounds in less than a week
- Extended IP protection



Ongoing U.S. Phase 2 Adaptive Design Study

A multicenter, prospective randomized assessor blinded study for treatment of venous leg ulcers

Study is ongoing

Interim assessment is anticipated in mid-year 2021

Study Objectives	Assess safety and efficacy of EscharEx compared to Gel Vehicle (placebo control) and non-surgical SOC*
Study Design	• Sample size: 120 VLU patients • Interim assessment for futility and potential sample size adjustment**
Endpoints	**Primary** Incidence of complete debridement of non-viable tissue vs. Gel Vehicle (placebo control) **Secondary** pain & wound area reduction; granulation tissue; wound QoL; time to complete debridement **Safety** Local and systemic safety and tolerability; incidence and time to wound closure

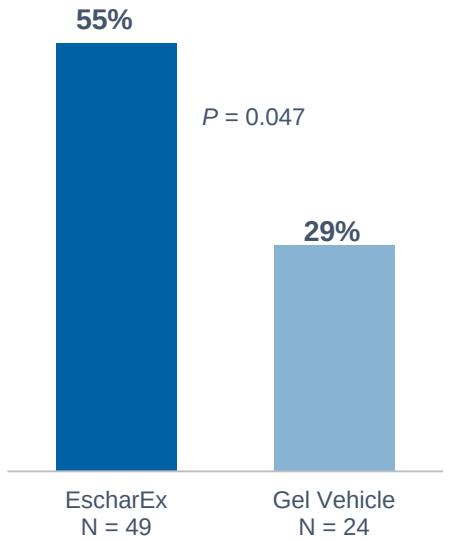
*Non-surgical standard of care – enzymatic or autolytic debridement
**Max. sample size = 160 patients

Phase 2 Study Successful Results

EscharEx ®

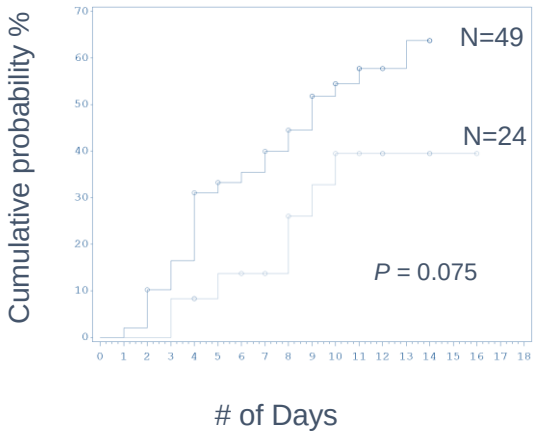
ITT Analysis

Incidence of complete debridement*



Significantly higher incidence of complete debridement

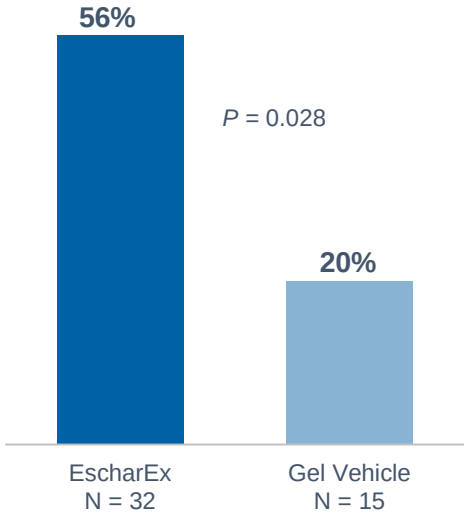
Time to complete debridement **



Shorter time to achieve complete debridement

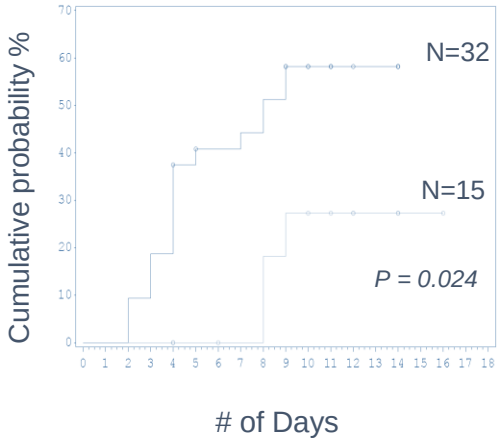
VLU's and DFU's Post-Hoc Analysis

Incidence of complete debridement*



Significantly higher incidence of complete debridement

Time to complete debridement **



Shorter time to achieve complete debridement

- Safety profile comparable to hydrogel vehicle and no deleterious effect on wound healing was observed
- No material safety concerns were identified in all doses and dosing regiments

>90% of the patients who completed debridement with EscharEx were debrided within 7 days (after 4-5 daily applications)

MediWound

*w/i up to 10 daily applications
**Kaplan-Meier survival analysis with log rank p-value

Pharmacology study

Pharmacology study

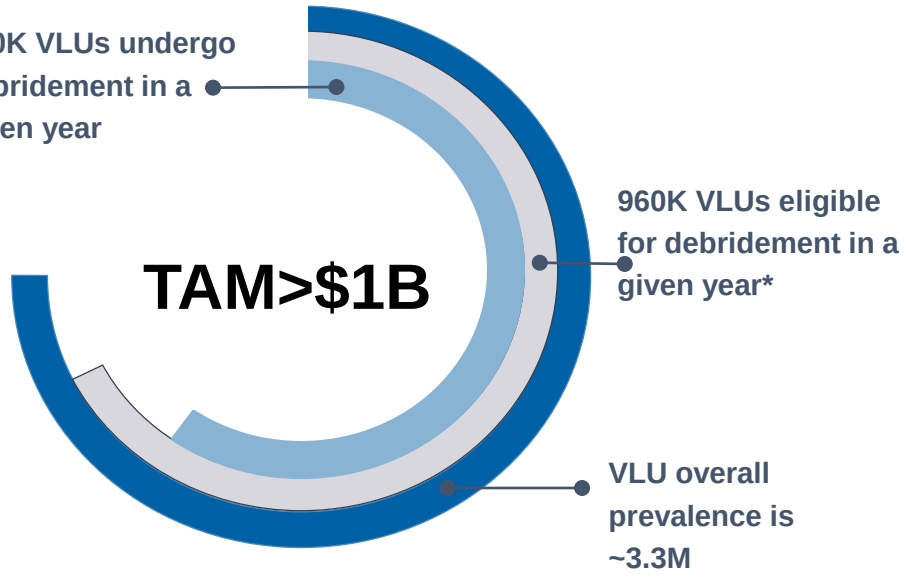
Conducted in US

Data expected in 2H 2021

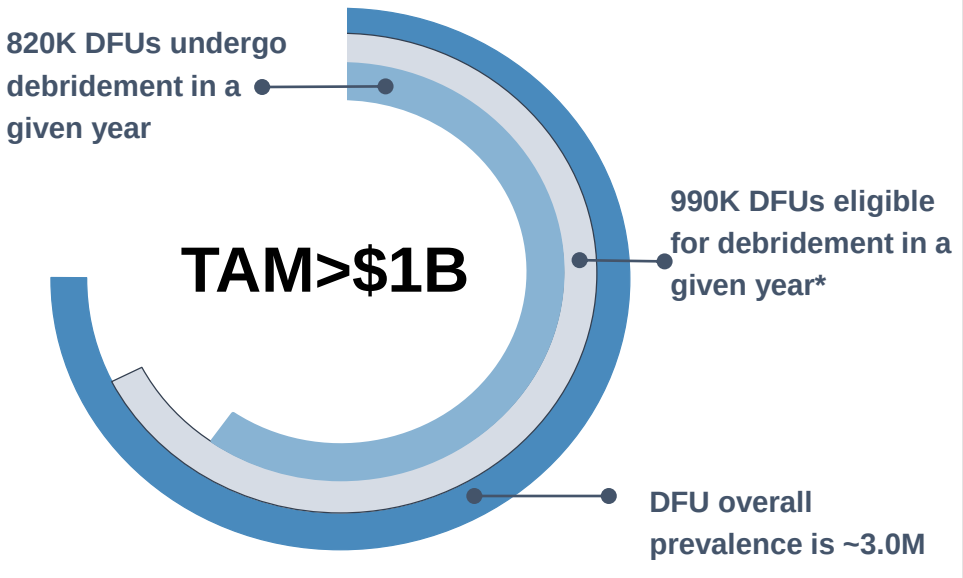
Study Objectives	Assess the pharmacological effect of EscharEx in patients with VLU and DFU
Study Design	• Single arm • Open label • Up to 15 patients
Data Collection	**Clinical performance** Safety and efficacy **Effect on biofilm** Reduction of biofilm burden **Anti- Inflammation** Inflammation reduction **Wound progression** Wound bed preparation

U.S. Debridement Market Opportunity

2019 US VLU Epidemiology Estimate



2019 US DFU Epidemiology Estimate



Feedback supports potential to extrapolate beyond initial indication given similarities of debridement approaches

MediWound

Source: Huron Primary Research (2019)
* Including 45% recurrence

Commercial Strategy

Target Audience

Site of care:

- Hospital-based outpatient department
- Wound care clinics
- Skilled nursing facilities
- Home care

Key clinicians:

- Vascular specialists
- Plastic surgeons
- Podiatrists
- Primary care physicians

Pricing

- Current enzymatic debridement average cost of treatment estimated at $1,600-$2,000
- Pricing to reflect cost saving

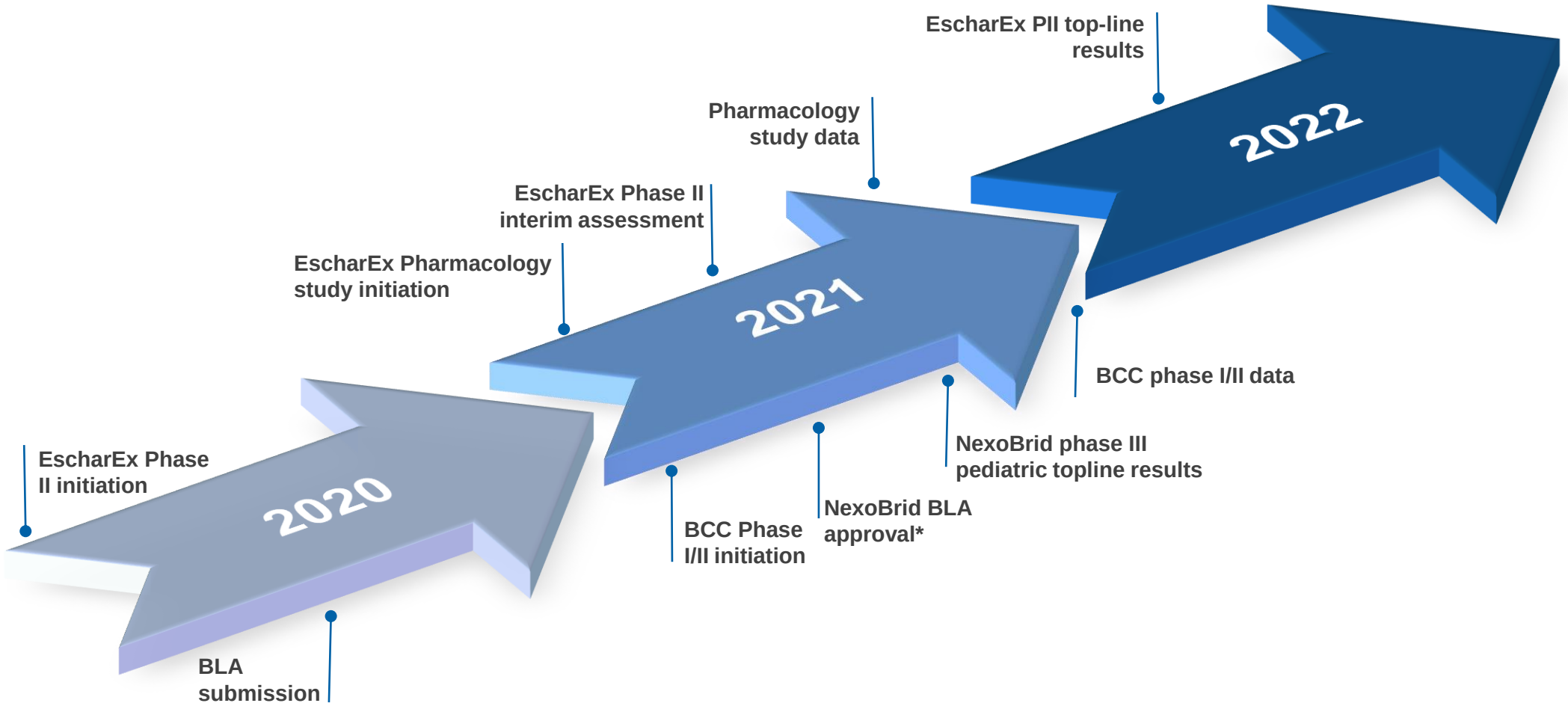
Reimbursement

- Existing reimbursement codes for enzymatic debridement
- Hospital Outpatient Prospective Payment System (OPPS) code 97602:

"Removal of devitalized tissue from wound(s), non-selective debridement, without anesthesia (e.g., wet-to-moist dressings, enzymatic abrasion), including topical applications(s), wound assessment, and instruction(s) for ongoing care, per session."

Source: Huron Primary Research (2019)

Upcoming Milestones



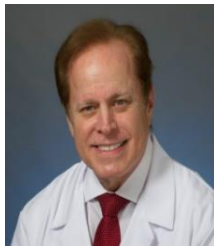
*subject to FDA approval

Experts Panel Discussion

Robert S. Kirsner, M.D., PhD
Chairman & Harvey Blank Professor
Dr. Phillip Frost Department of Dermatology & Cutaneous Surgery
Professor of Public Health Sciences
Director, University of Miami Hospital and Clinics Wound Center
University of Miami Miller School of Medicine

Ilina Sen
Life Sciences Sr. Director,
Huron Consulting Group

Adam Singer MD
Professor and Vice Chairman for Research
Department of Emergency Medicine
Stony Brook University



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Past President, Association for the Advancement of Wound Care
Past President, American Board of Wound Management