Development of a Porcine Hard-to-Heal Wound Model and Evaluation of a Bromelain-Based Enzymatic Debriding Agent

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Disclosures

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- Dr. Shoham and Dr. Singer are medical consultants for MediWound

Hard-to-Heal Wounds: The Need for Animal Model

- Chronic wounds are common and hard to heal
- Development of new therapies is limited by lack of chronic, hard to heal preclinical wound model

Objectives of current study:

- Develop a standardized hard-to-heal porcine wound model
- Assess the debridement efficacy of bromelain-based debridement (BBD) vs. collagenase using this porcine model

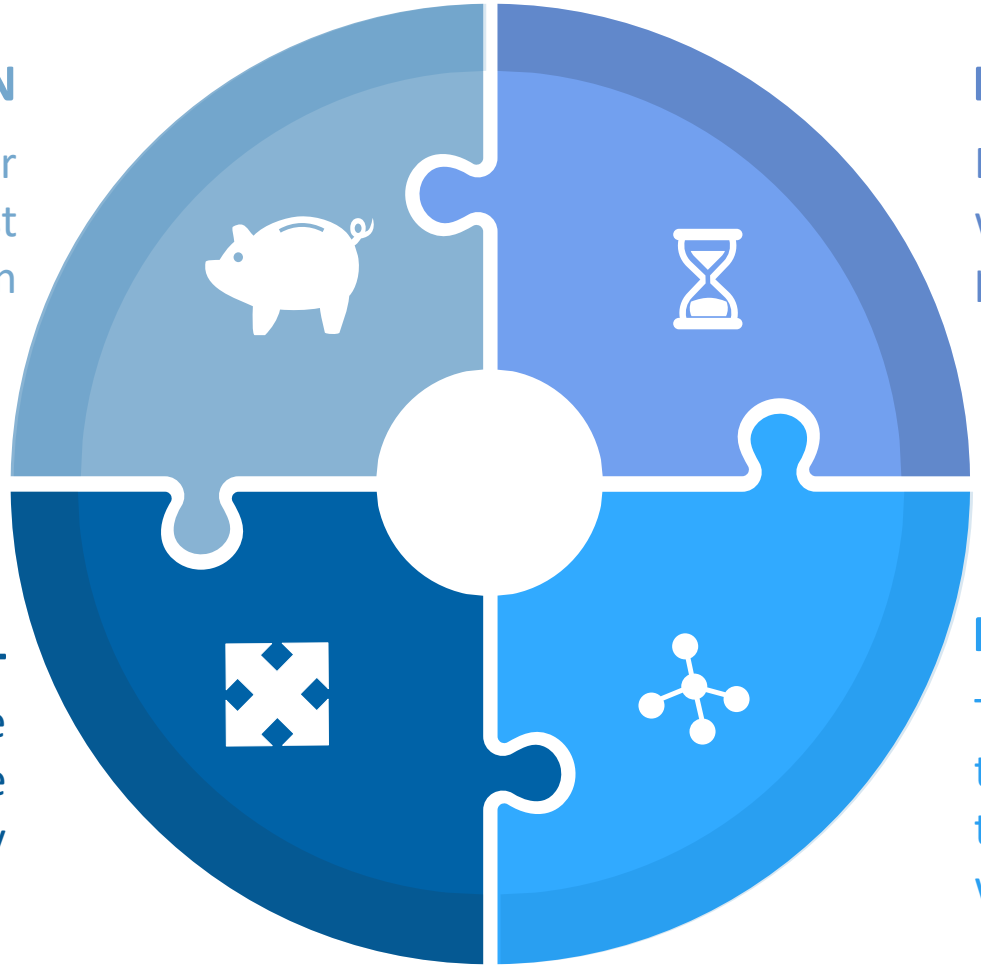
Key Considerations for Developing a Hard-to-Heal Wound Model

SIMILARITY TO HUMAN SKIN

The preferred animal model for cutaneous research is one that most closely resembles human skin structure

DELAYED WOUND CLOSURE

Delayed healing to maintain the wound open during the debridement process



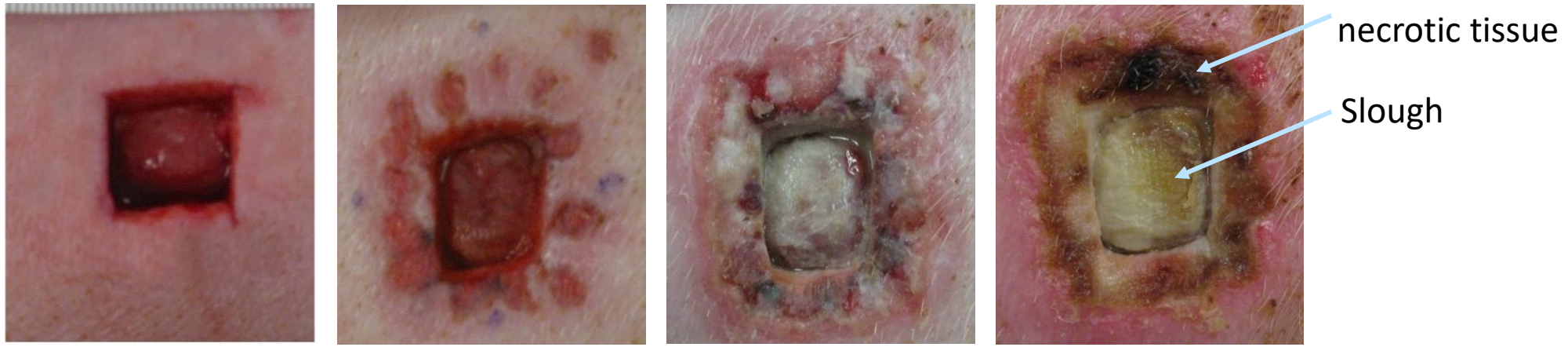
LARGE ANIMAL

Using a large animal allows for the creation of multiple wounds on the same subject, minimizing variability caused by individual differences

NECROTIC TISSUE AND SLOUGH

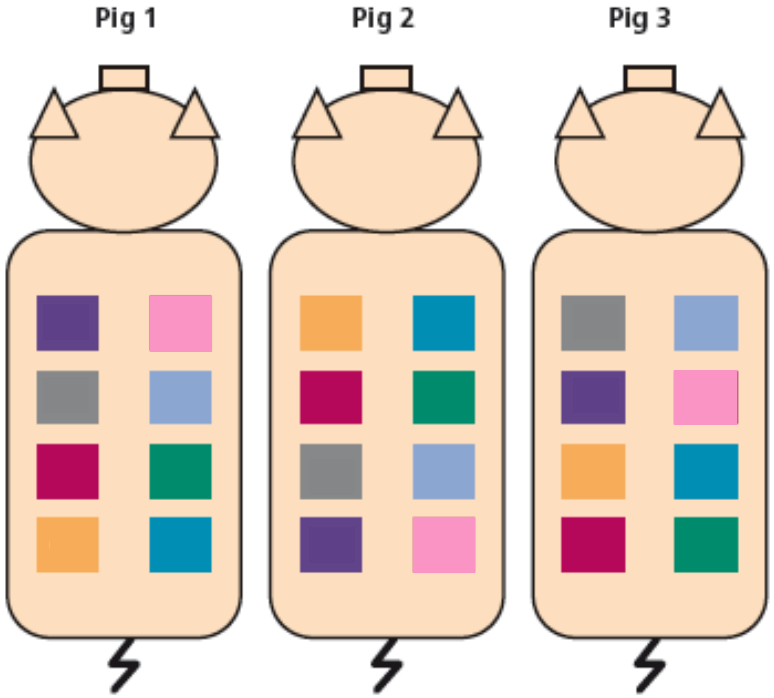
The wound should be covered with the main components of necrotic tissue found in hard-to-heal human wounds

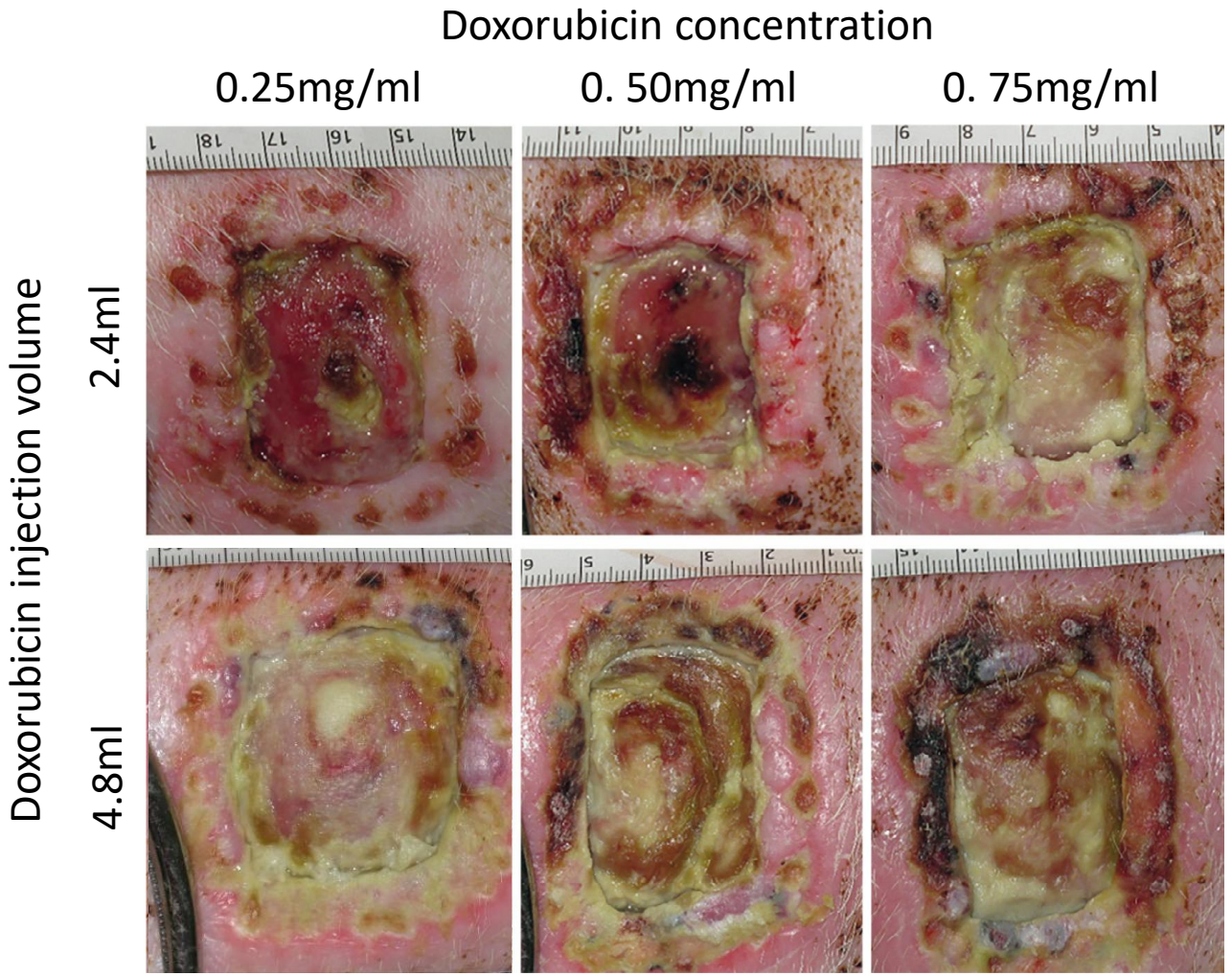
Establishing a Pig Model for Hard-to-Heal Wounds



Establishing a Pig Model for Hard-to-Heal Wounds

The model establishment study ensured an equal distribution of test groups across animals and between locations near the head and tail (each test group is represented by different color)

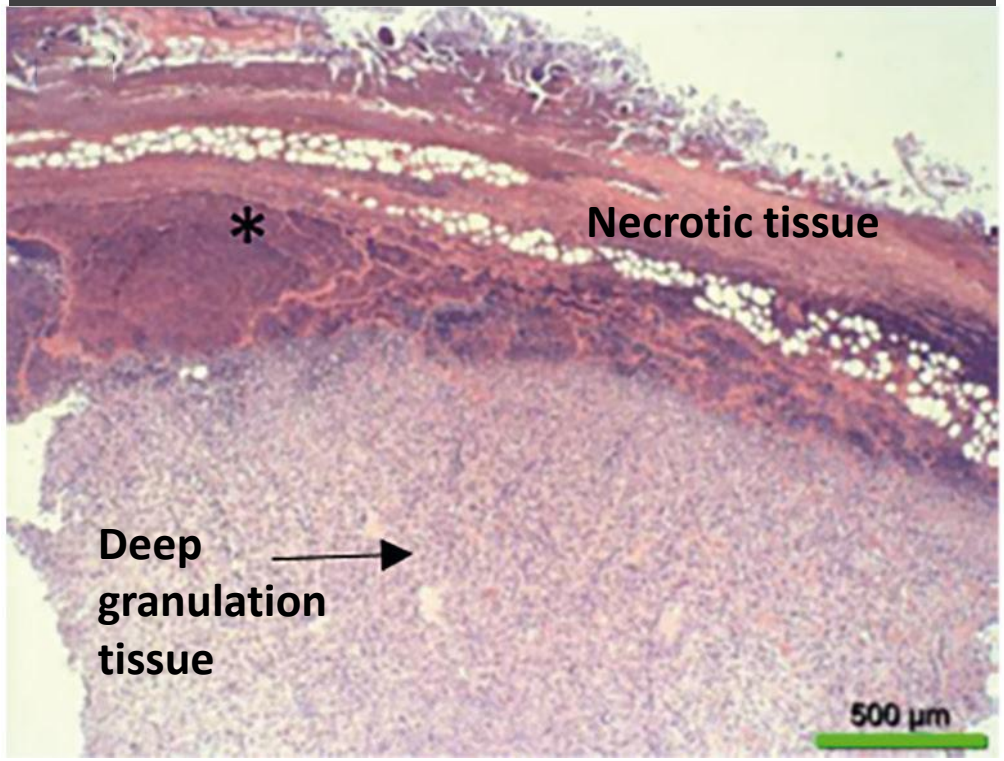




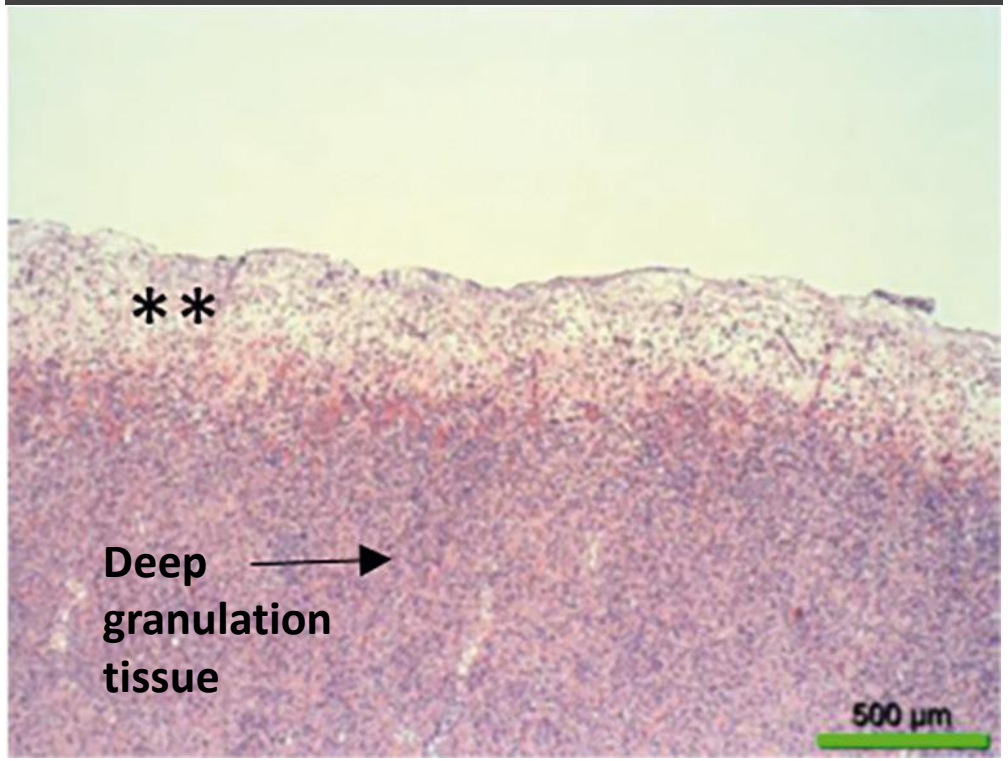
Histology of the Wound in the Model

Representative micrograph of H&E-stained tissue taken from the wound

Wound periphery



Wound center



* Infiltrate rich in inflammatory cells

** Edematous granulation tissue

Hard-to-Heal Wound Model Properties

SIMILARITY TO HUMAN SKIN

The **pig** is the preferred animal model for cutaneous research due to it similarity to the human skin structure

DELAYED WOUND CLOSURE

The model allows the wound to remain open for **~40 days**, enabling evaluation of the product during this period

LARGE ANIMAL

The pig allows for the creation of **10 wounds** on the same animal, ensuring multiple test groups are represented on each animal. This helps minimize variability caused by animal differences

NECROTIC TISSUE AND SLOUGH

The wound is covered both by **full-thickness necrotic tissue** at the wound periphery and **slough** at the center, similar to human hard to heal wound

Comparison Of BBD To Enzymatic Standard Of Care

BBD – Bromelain Based Debridement

Investigational drug - **Phase 3 ongoing**

Bromelain-enriched enzymatic mixture; derived from pineapple plant; **Multiple** targets of action

Use: **1-2 weeks**, daily; Monotherapy

Same active ingredient as **NexoBrid®, approved by FDA/EMA** for eschar removal in burns

Phase 2 trials showed **superiority over** placebo (gel vehicle) and **non-surgical standard of care** [3,4].

Collagenase Ointment

Approved in the US **in the 1960s** for debriding chronic dermal ulcers and severely burned areas

Collagenase; **Single** target of action (collagen)

Use: **4-8+ weeks**, daily; Typically coupled with sharp debridement [1,2]

"There is a **lack of RCTs** with adequate methodological quality"[2]

Clinical trials mostly showed improvements compared to baseline, **not superiority vs. standard of care** [1,2]

1. Lantis JC and Gordon I. *Wounds* 2017; **2. Patry et al.** *International Wound Journal* 2017; **3. Shoham et al**. *Wound Rep Reg* 2021;
4. Snyder et al. *Wounds* 2023

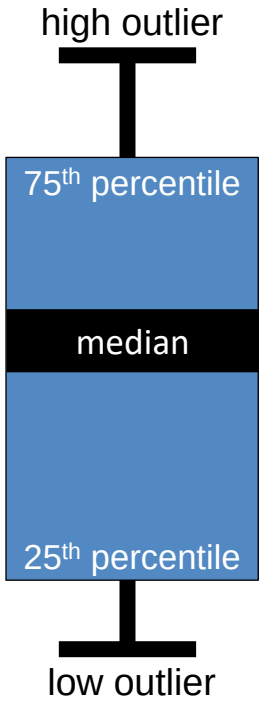
BBD vs. Enzymatic Standard of Care

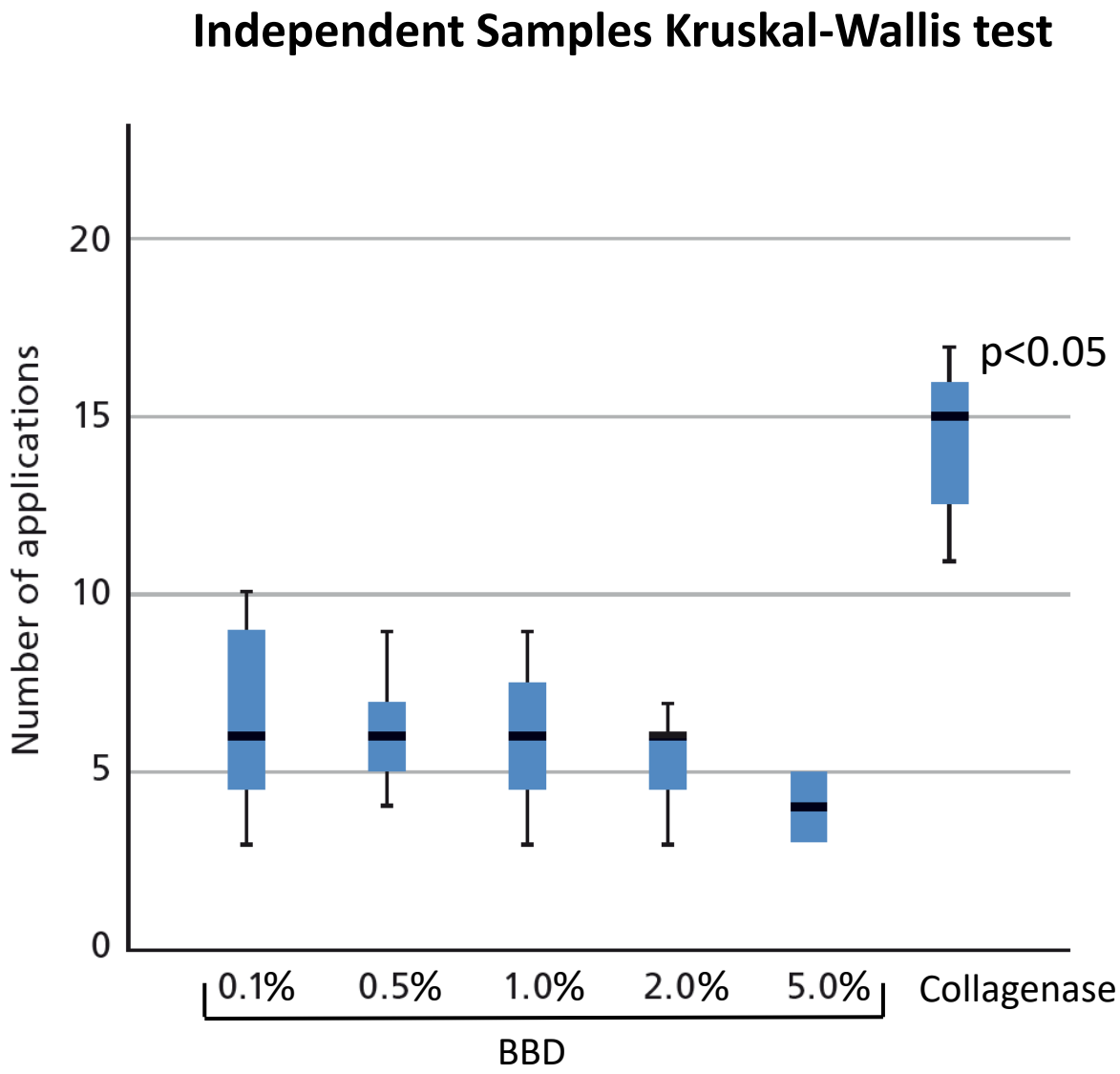
Incidence of Complete (>95%) Debridement

Number of daily applications	Collagenase (n=11)	BBD 0.1% (n=7)	BBD 2% (n=7)
4	0/11 (**0%**)	2/7 (**29%**) *p*=0.14	1/7 (**14%**) *p*=0.39
7	0/11 (**0%**)	4/7 (**57%**) *p*=0.01	7/7 (**100%**) *p*<0.001
10	0/11 (**0%**)	7/7 (**100%**) *p*<0.001	7/7 (**100%**) *p*<0.001
12	3/11 (**27%**)	7/7 (**100%**) *p*=0.004	7/7 (**100%**) *p*=0.004

P values represents comparison of BBD to collagenase

BBD vs Collagenase: # of Applications to Achieve Complete Debridement





Subgroup Analysis from a Phase 2 RCT in VLU Patients

Comparable Baseline Characteristics

Parameter	BBD (n=46)	Collagenase (n=8)
Age (years) - Mean (SD)	65.5 (12.2)	59.9 (11.7)
Female Gender - n (%)	20 (43.5%)	4 (50.0%)
Wound Age (weeks) - Mean (SD)	26.8 (20.5)	29.1 (27.9)
Wound Size (cm^2) - Mean (SD)	13.3 (20.4)	10.3 (5.7)
Non-Viable Tissue (%) - Mean (SD)	72.2 (13.7)	78.1 (15.8)

Kirsner RS, et al. EClinicalMedicine. 2024;66:100829**; Dove CY**, Wounds. 2025 – In Press

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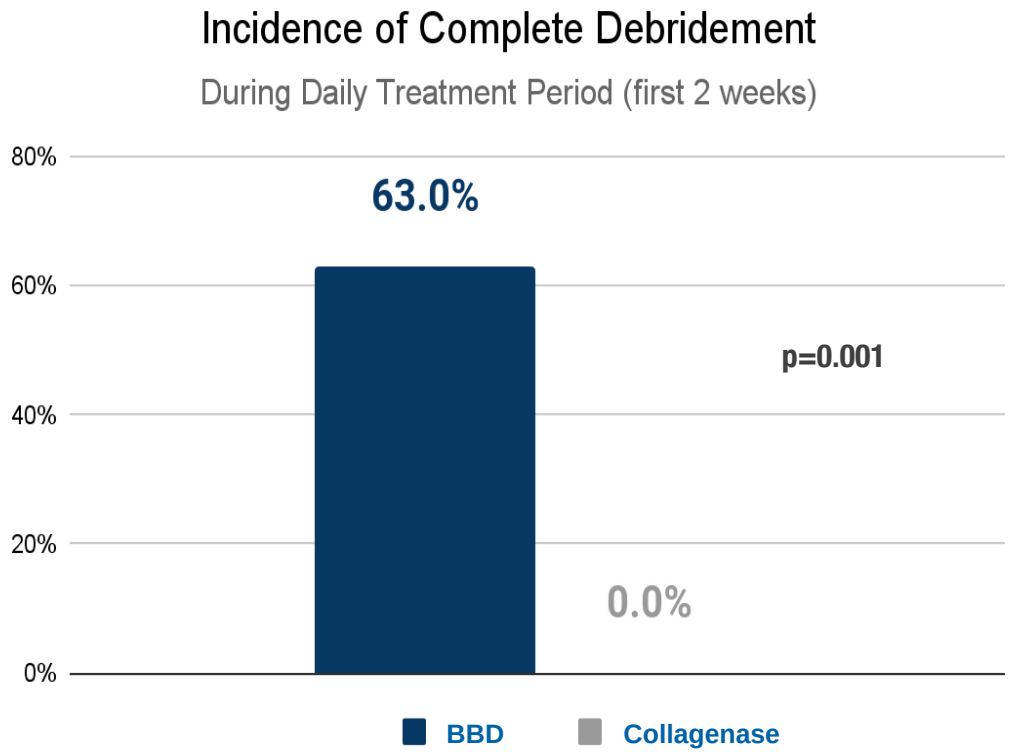

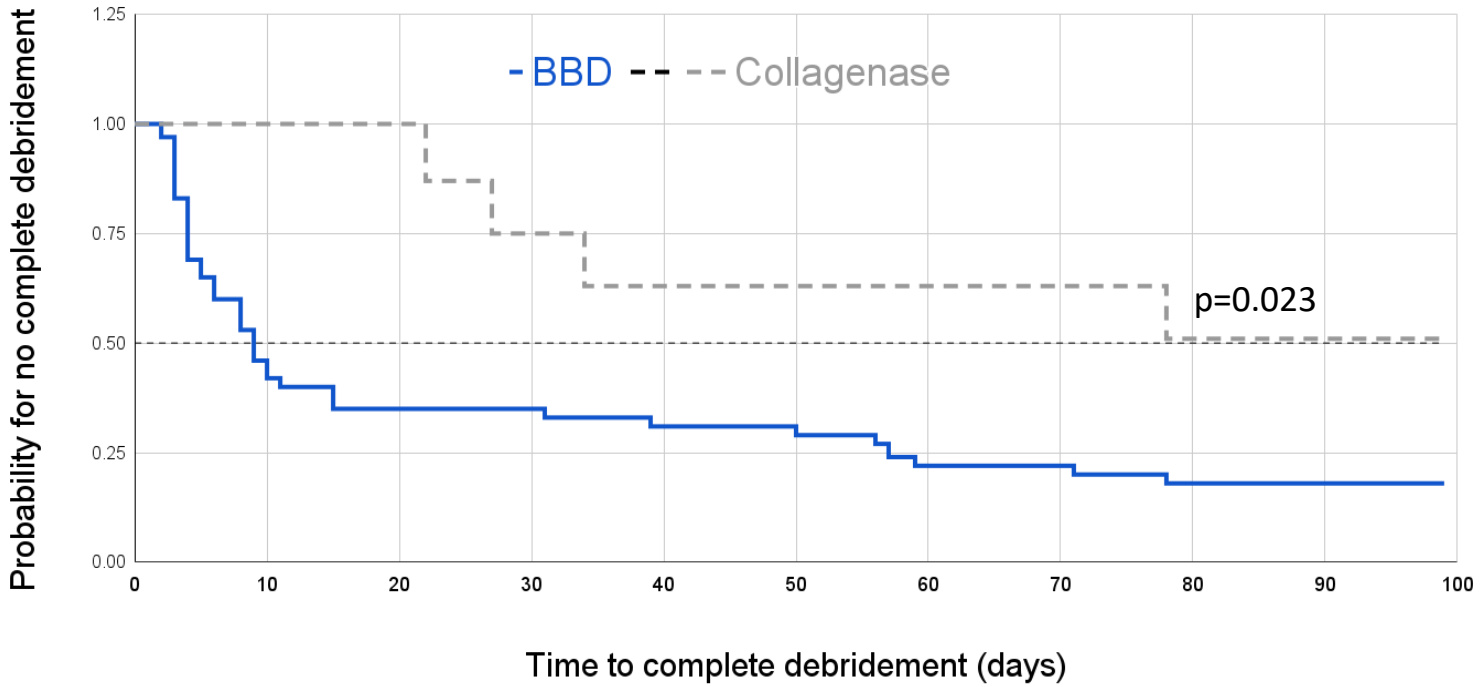

Estimated median time to achieve complete debridement	
BBD	**Collagenase**
9 days (95% CI=5-15 days)	**not achieved** (95% CI=22-Not Applicable)

p=0.023

Case studies from a Phase 2 RCT in VLU patients

BBD

S204-013

Baseline

After 1st application

End of Daily Applications
Complete debridement - 3 applications

Collagenase

S204-005

Baseline

After 1st application

End of Daily Applications
8 applications

Summary

- We established a standardized porcine hard-to-heal wound model
- The wound model demonstrated the superiority of BBD over collagenase in debriding hard to heal wounds
- Similar results were obtained in subgroup analysis from a phase 2 RCT in VLU patients

Questions?