Development of Porcine Fibula Fracture-Related Infection Model for Prolonged Field Care Studies

Presenter: Dena Norouzi, PhD Candidate

Funded by MTEC (MTEC-24-01-MPAI-031).

MHSRS 2026

NOTICE

Disclosures and disclaimers

The presenters (Dena Norouzi, BS) has no conflict to report.

The views expressed in this abstract are those of the authors and do not necessarily reflect the official policy or position of the Defense Health Agency, Department of War, nor the U.S. Government.

The experiments reported herein were conducted in compliance with the Animal Welfare Act and per the principles set forth in the "Guide for Care and Use of Laboratory Animals," Institute of Laboratory Animals Resources, National Research Council, National Academy Press, 1996.

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AGENDA

Presentation roadmap

01 **Background**
Fracture-related infection and the prolonged field care challenge

02 **Study Aim**
Main objective

03 **Methods**
Combat-relevant porcine FRI model

04 **Results**
Systemic and local bacterial bioburden at 72 h

05 **Discussion**
Interpretation, translational relevance, and limitations

06 **Conclusions & Next Steps**
Translational implications and future directions

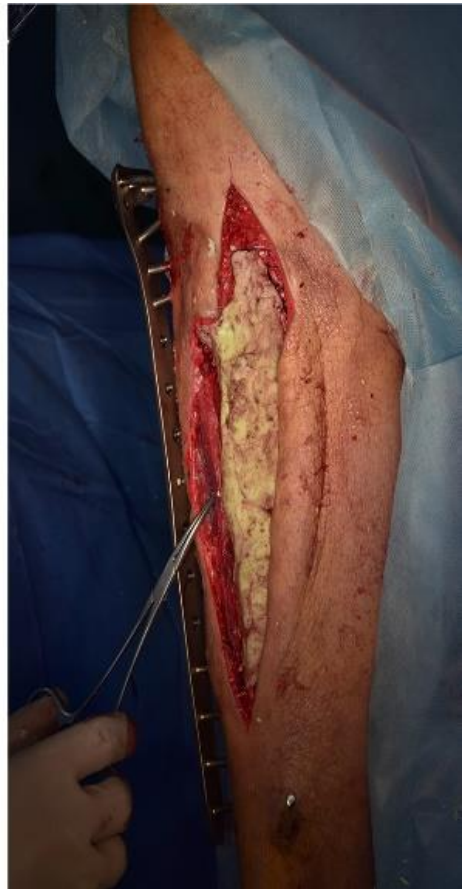
Fracture-related infection (FRI)

An Infection →
- **At the fracture site**
- **Around fixation hardware**

After fracture injury or surgical fixation

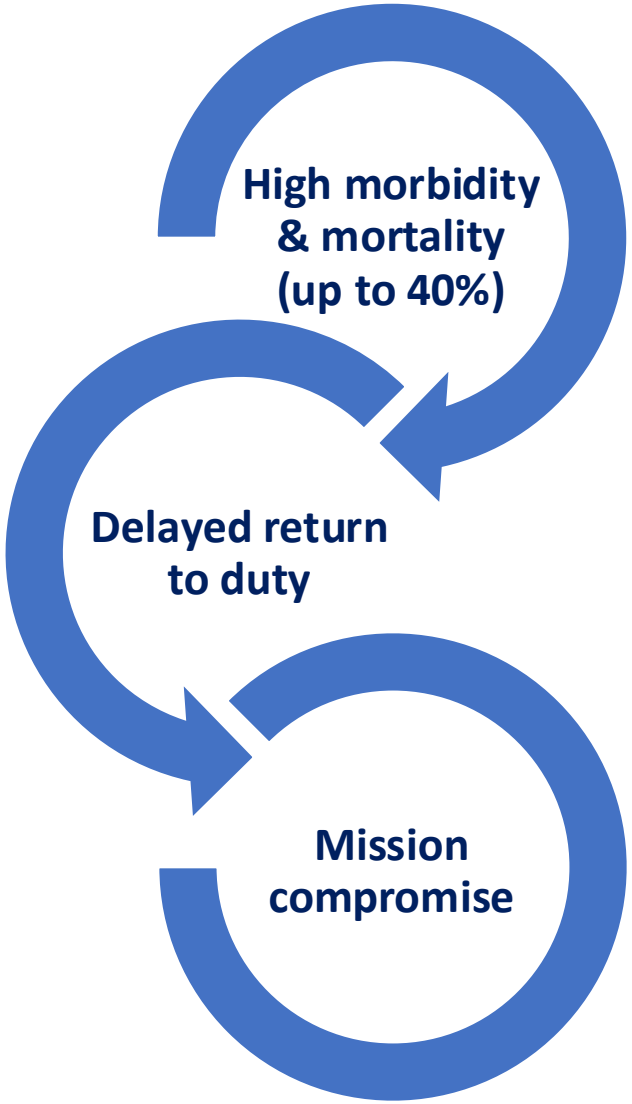
How do we diagnose? →
- Clinical signs
- Inflammatory markers
- Microbiological confirmation

How do we manage? →
- Multidisciplinary debridement
- Targeted antibiotics



Adapted from: TCCC Guidelines for Hemorrhage Control, Joint Trauma System (2024); FRI consensus definitions.

The Burden of Fracture-Related Infection



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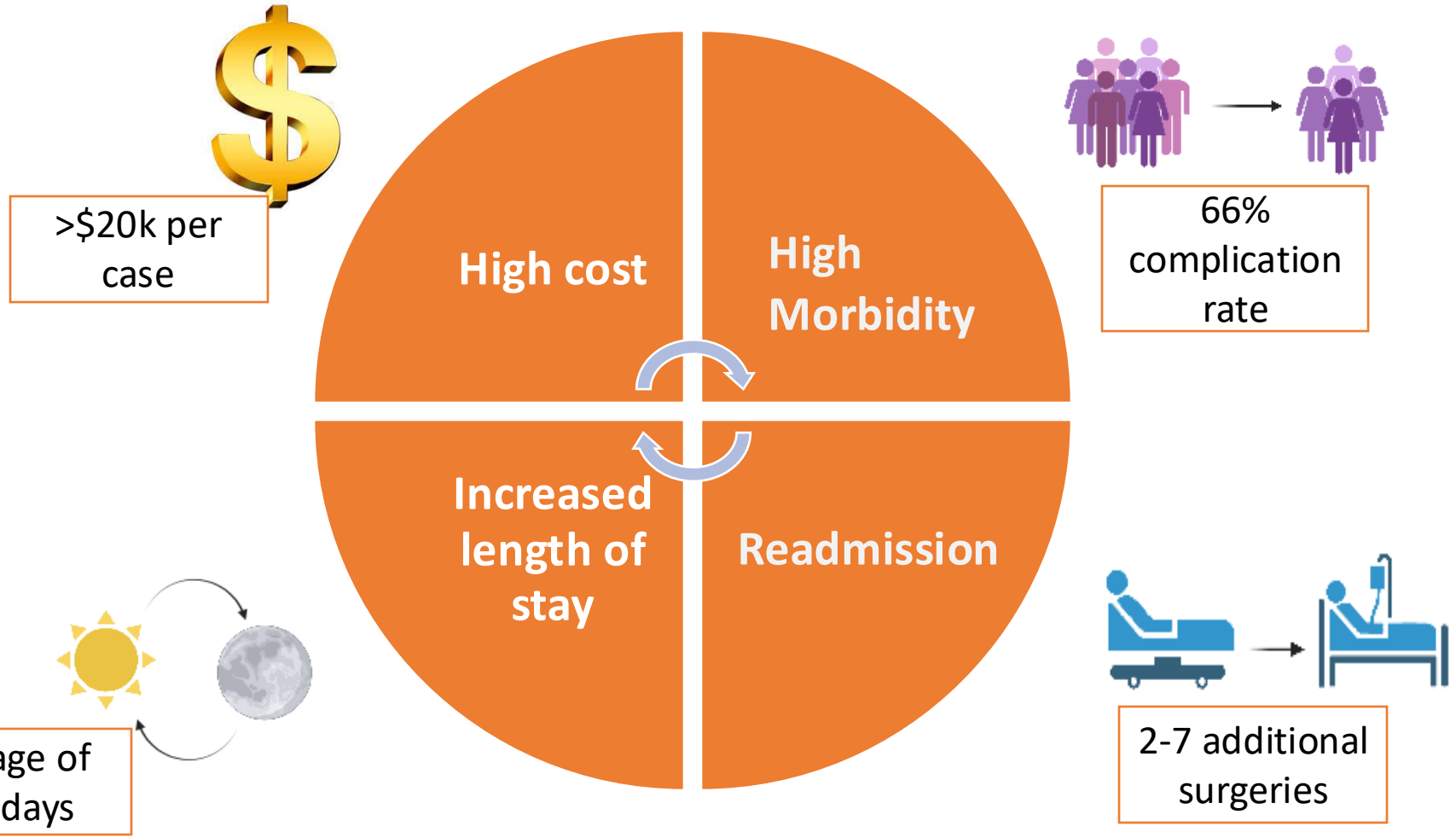
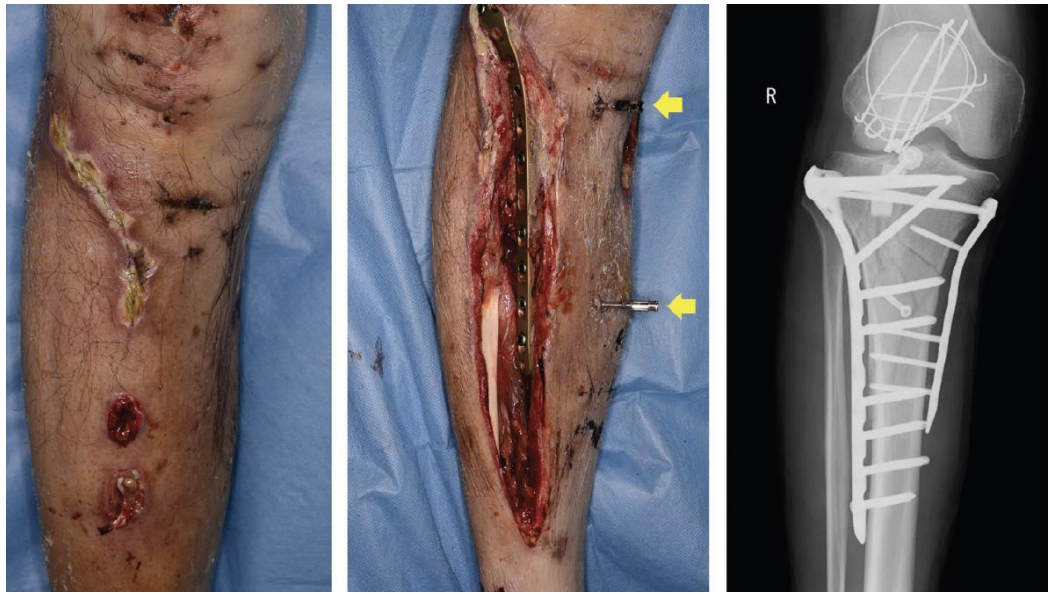


Adapted from: TCCC Guidelines for Hemorrhage Control, Joint Trauma System (2024).

The problem

Infectious complications frequently occur following combat-related extremity trauma.



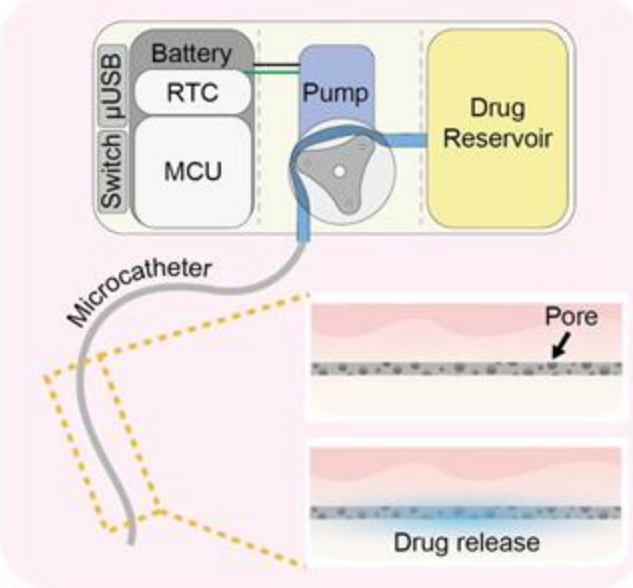
Adapted from: Orthopaedics & Traumatology: Surgery & Research, 111(1, Suppl), 104055. https://doi.org/10.1016/j.otsr.2024.104055

DOD Research Gap/Focus area of the MTEC MPAI 2024 mechanisms

Combat Casualty Care: Technologies designed for use in harsh battle zones, such as easily transportable medical devices, forward surgical equipment, and treatments for severe wounds.

Overall Study Objective

Evaluate the efficacy of a bioabsorbable, porous catheter system for local antimicrobial delivery in FRI under prolonged field care conditions.



Journal of Infection
Volume 89, Issue 6, December 2024, 106312

Bacteria and Bacterial Diseases

Pandrug-resistant *Klebsiella pneumoniae* isolated from Ukrainian war victims are hypervirulent

Oskar Ljungquist [a 1], Michal Magda [b 1], Christian G. Giske [c d], Chaitanya Tellapragada [d], Oleksandr Nazarchuk [e f], Dmytro Dmytriiev [e g], Oskar Thofte [h], Valdemar Öhnström [h], Erika Matuschek [i], Anna M. Blom [b], Kristian Riesbeck [h j 2]

Today's Focus

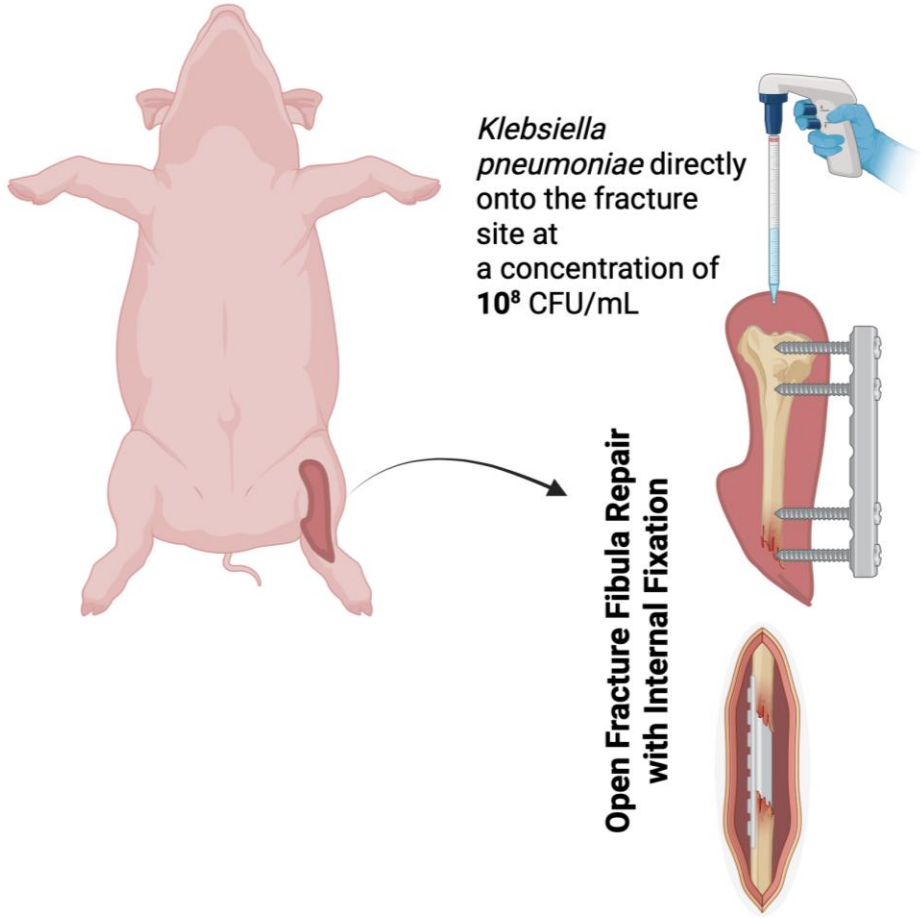
A combat-relevant porcine fibula model inoculated with *K.pneumoniae* will reproducibly generate local bacterial bioburden and biofilm without early systemic comprise, supporting its use as a preclinical countermeasure-testing platform.

METHODS

Combat-relevant porcine FRI model

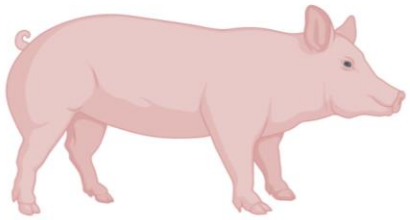
Clinically relevant model

1. Fibula fracture with periosteal defect and soft tissue injury created on the right hindlimb of Yorkshire pigs (55–75 kg. M/F).
2. Fracture stabilized with a 5-hole one-third tubular plate.
3. *K. pneumoniae* (ATCC 13883, 10^8 CFU/mL) applied evenly to the site of fracture to closure.
4. Animals recovered and monitored for 72 h, with twice-daily veterinarian-approved pain and mobility assessment.
5. Bacterial bioburden quantified in wound fluid, fibula, orthopaedic implant, muscle, and bone marrow at 72 h.

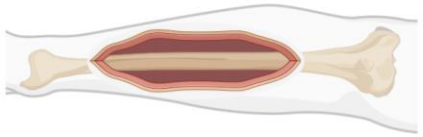


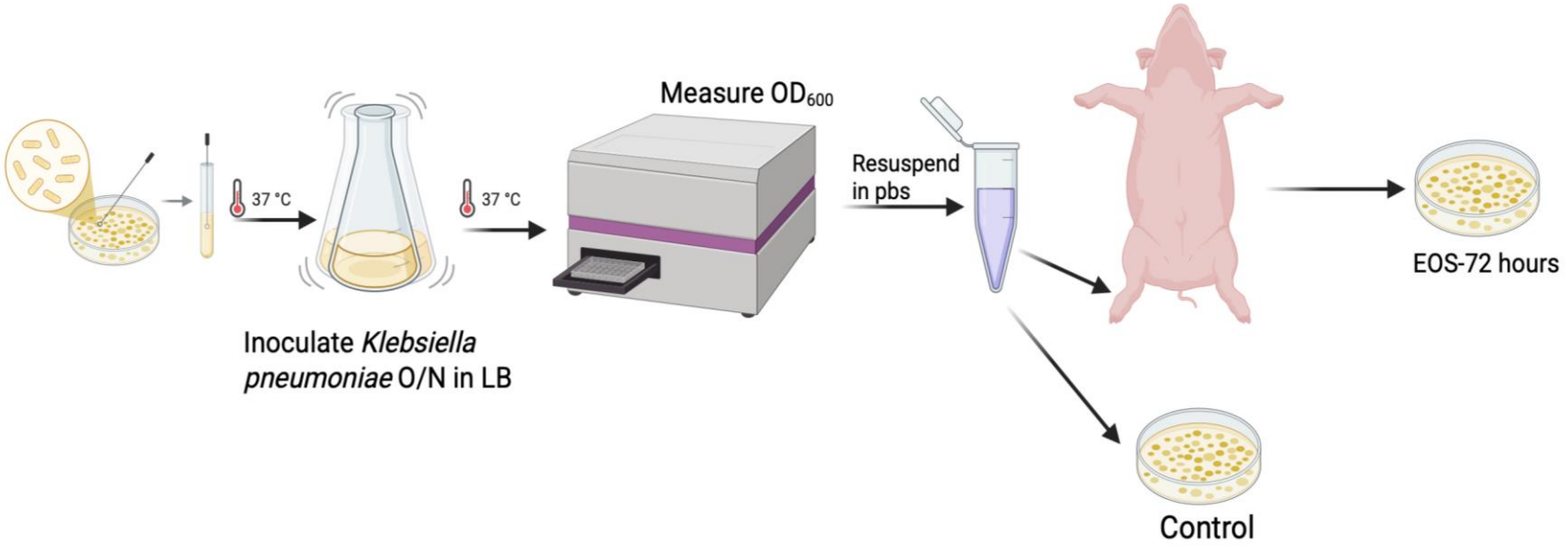
In Vitro Inoculum Prep

Model System:

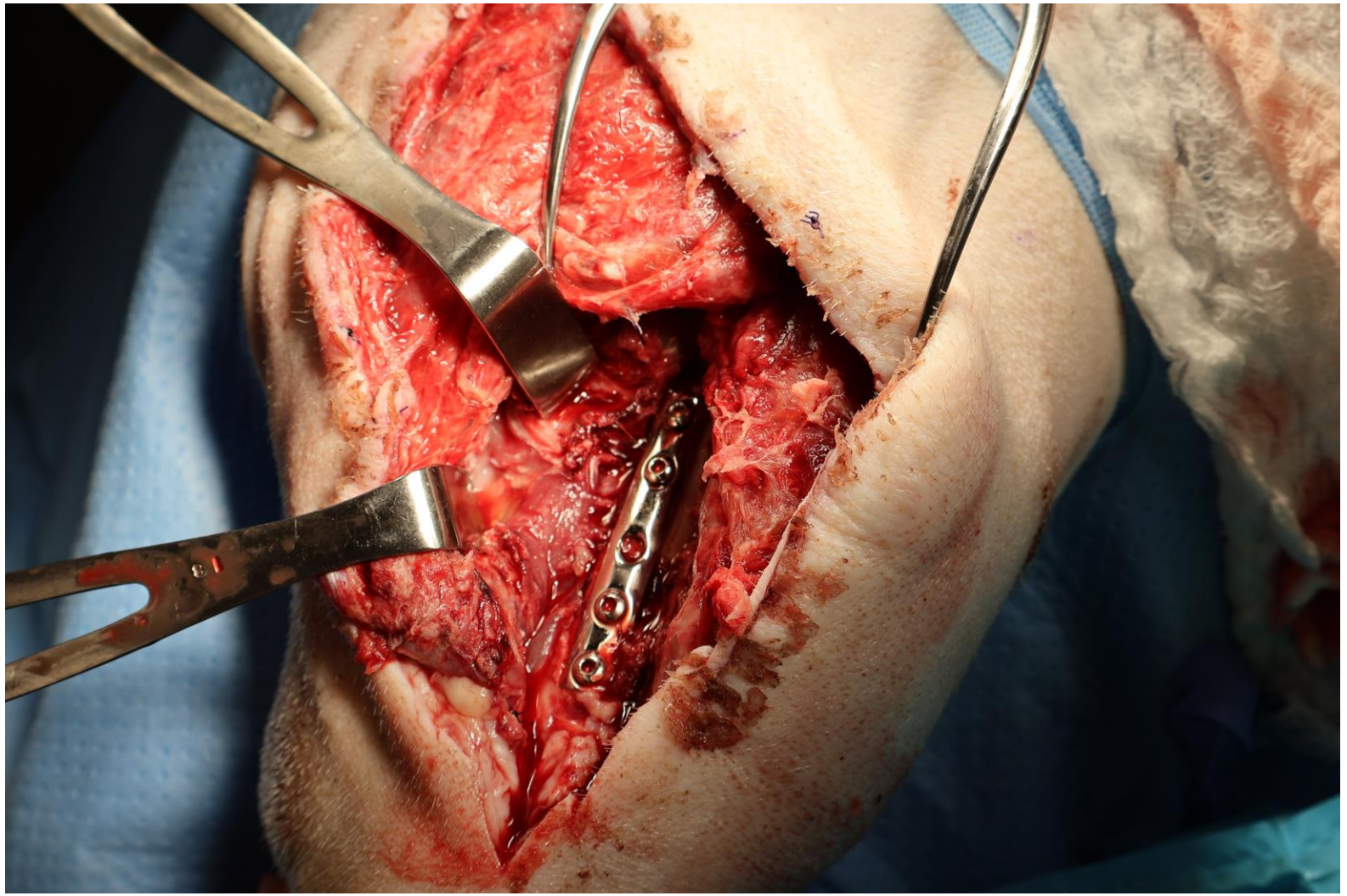


Open Fracture
Fibula Repair





Surgical Model: Fracture Fixation



Orthopaedic plate is placed at the site of injury for fracture fixation

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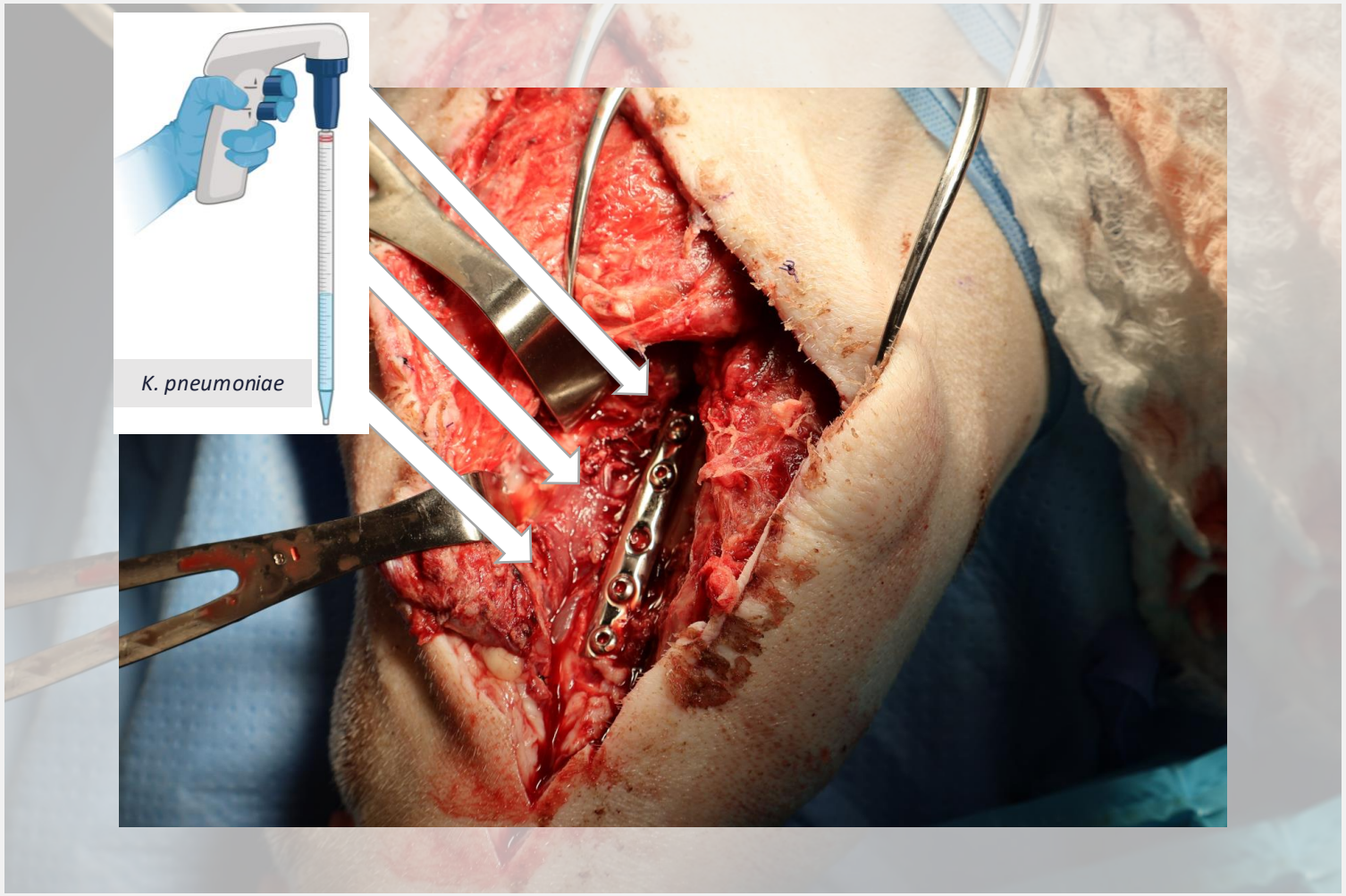

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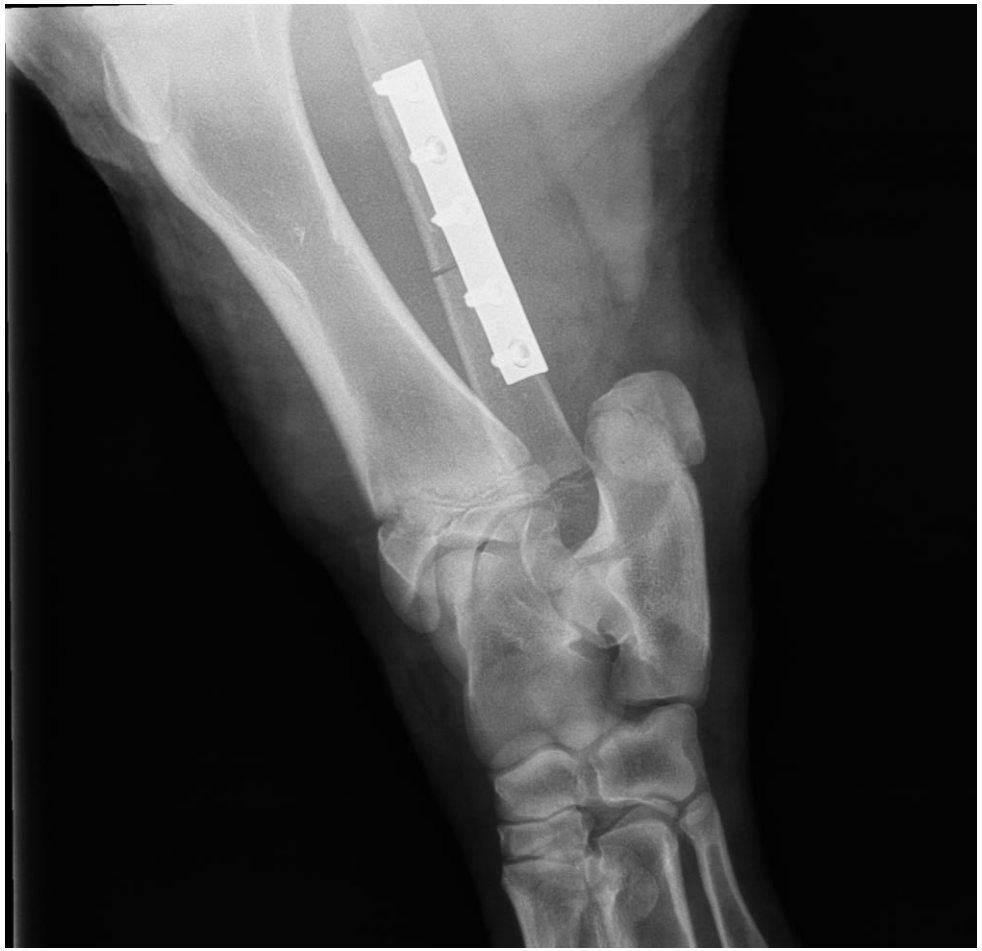
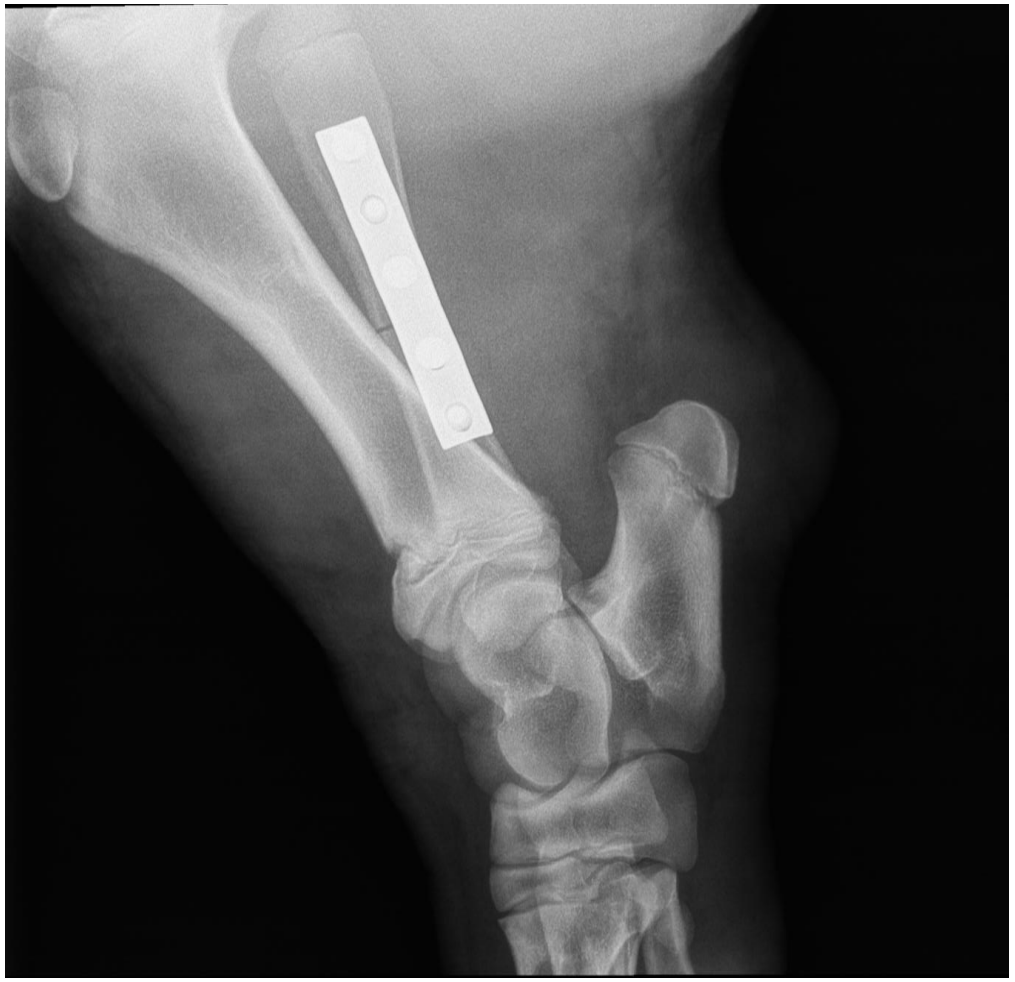
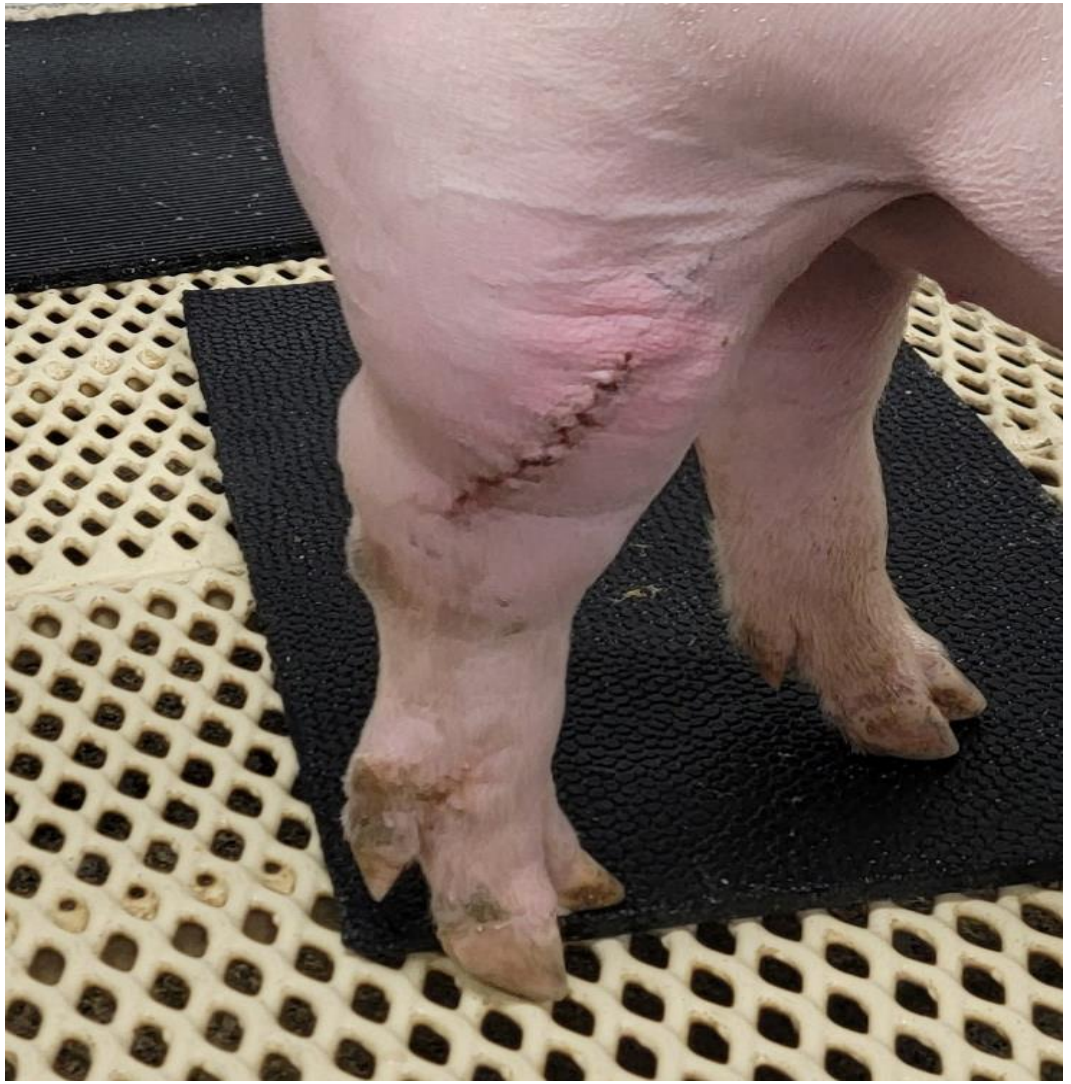


Post-fixation X-ray
Fibula fracture stabilized with orthopaedic plate



Hardware placement confirmation
Orthopaedic fixation maintained at surgical site at EOS (72h)

Surgical Model: After Surgery



Post-operative recovery

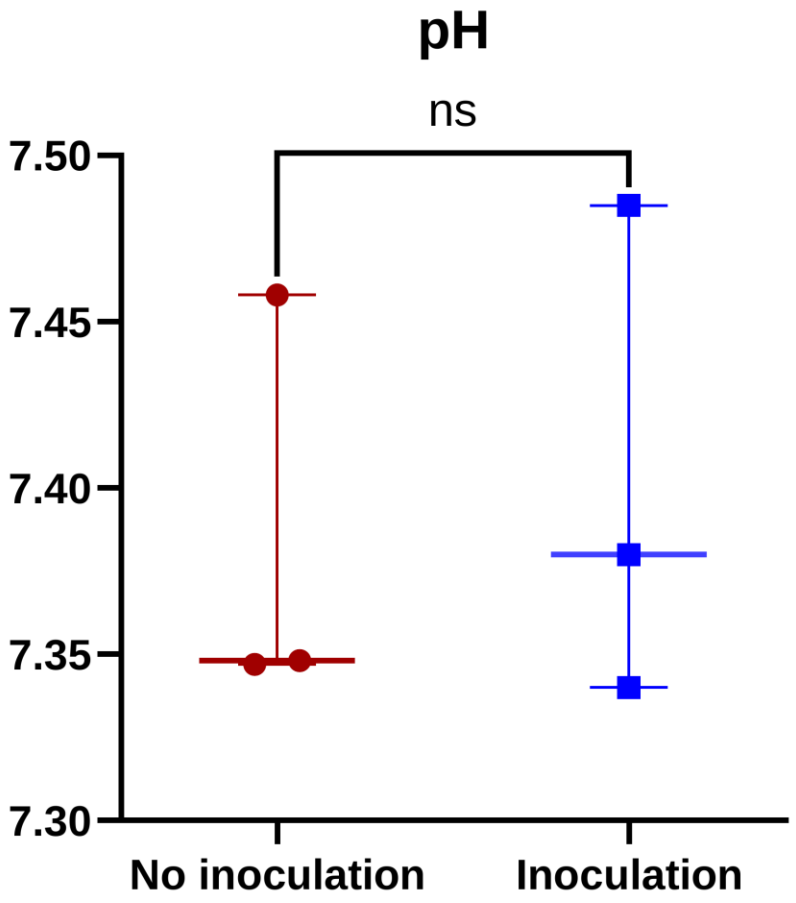
Early weight-bearing on the operated hindlimb

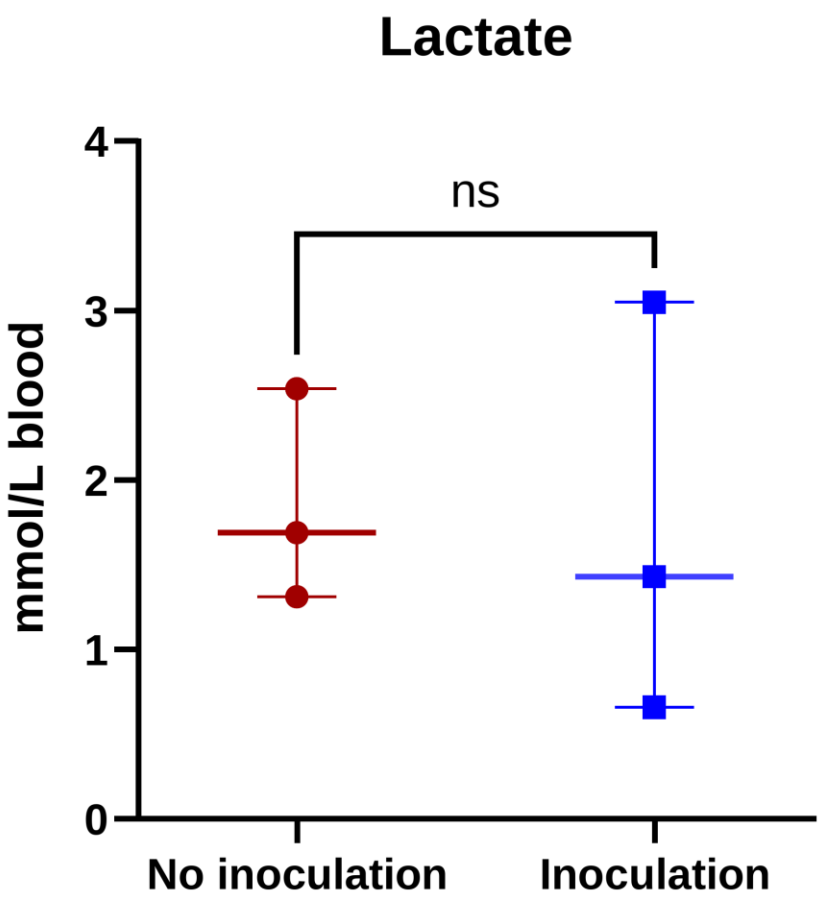
RESULTS · 01

Systemic Findings

Blood gas, metabolic, and hematologic response at 72 hours

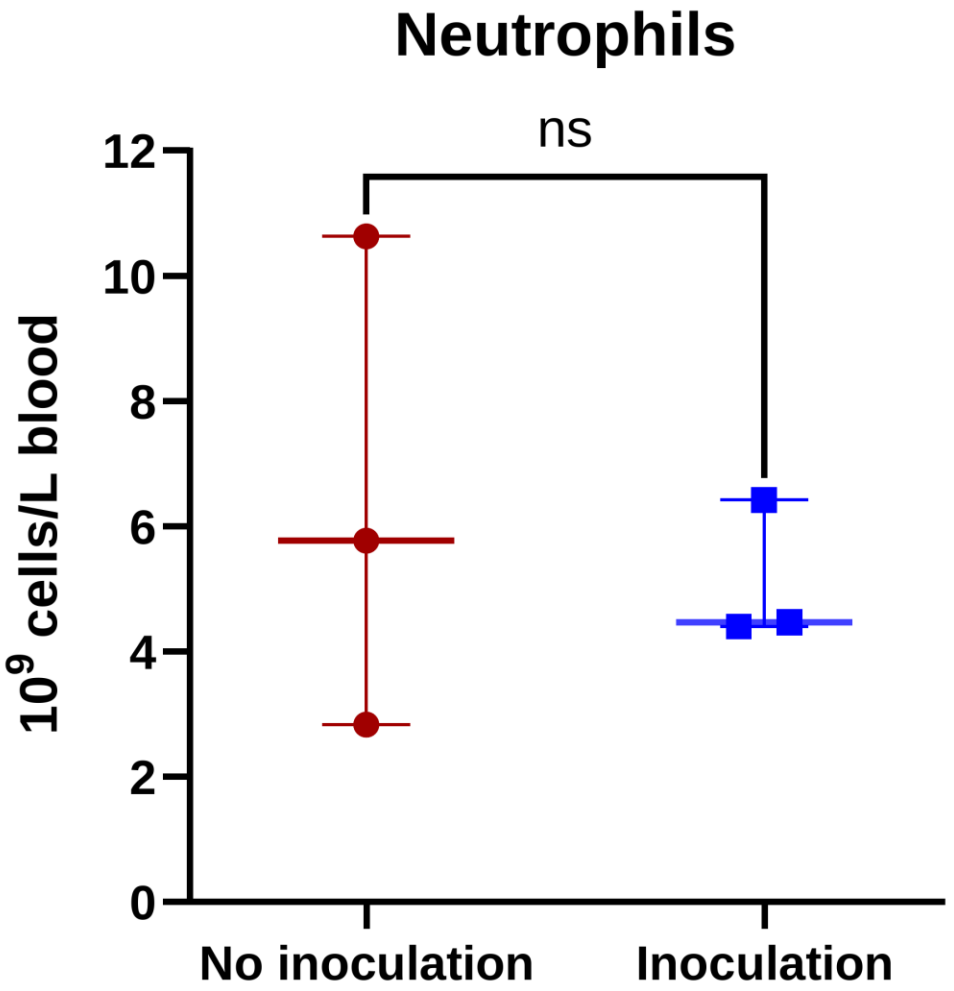
Acid–base and perfusion status





No significant difference in pH or lactate between groups — no evidence of systemic acidosis or impaired perfusion at 72 h.

Circulating neutrophils



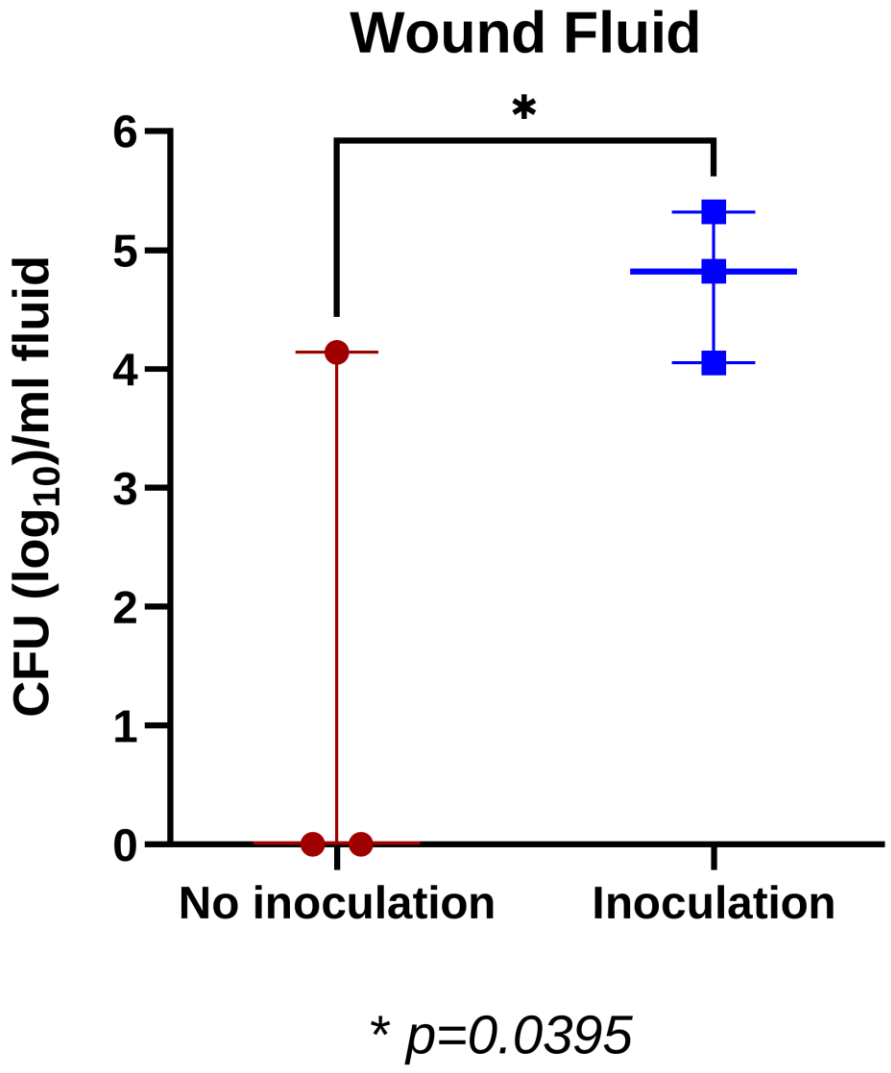
No significant difference in circulating neutrophils between groups, consistent with the absence of a systemic inflammatory response.

RESULTS · 02

Local Findings

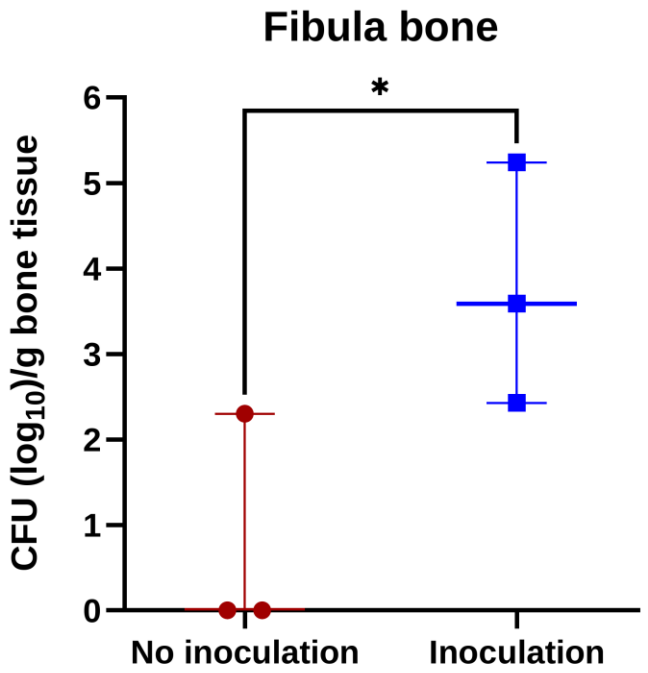
Bacterial bioburden at the site of injury

Planktonic bacteria in wound fluid

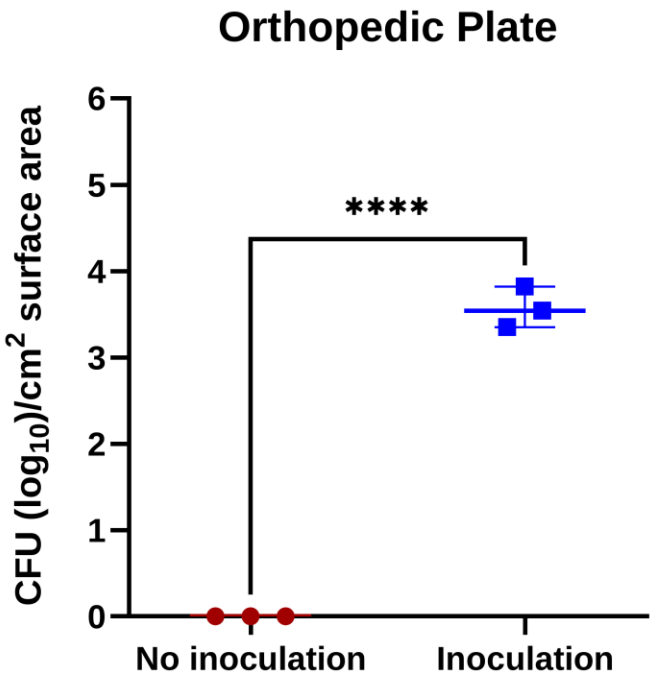


Inoculated wounds showed significantly higher planktonic bacterial burden than controls ($p = 0.0395$), confirming active infection.

Biofilm on bone and orthopaedic hardware



* *p=0.0279*



**** *p<0.0001*

Takeaway: Bacterial growth in bone and implant denotes biofilm. Inoculated animals showed significantly greater biofilm burden on fibula bone ($p = 0.0279$) and orthopaedic plate ($p < 0.0001$).

DISCUSSION

1. **A reproducible infection model that supports preclinical studies related to wound infection.**

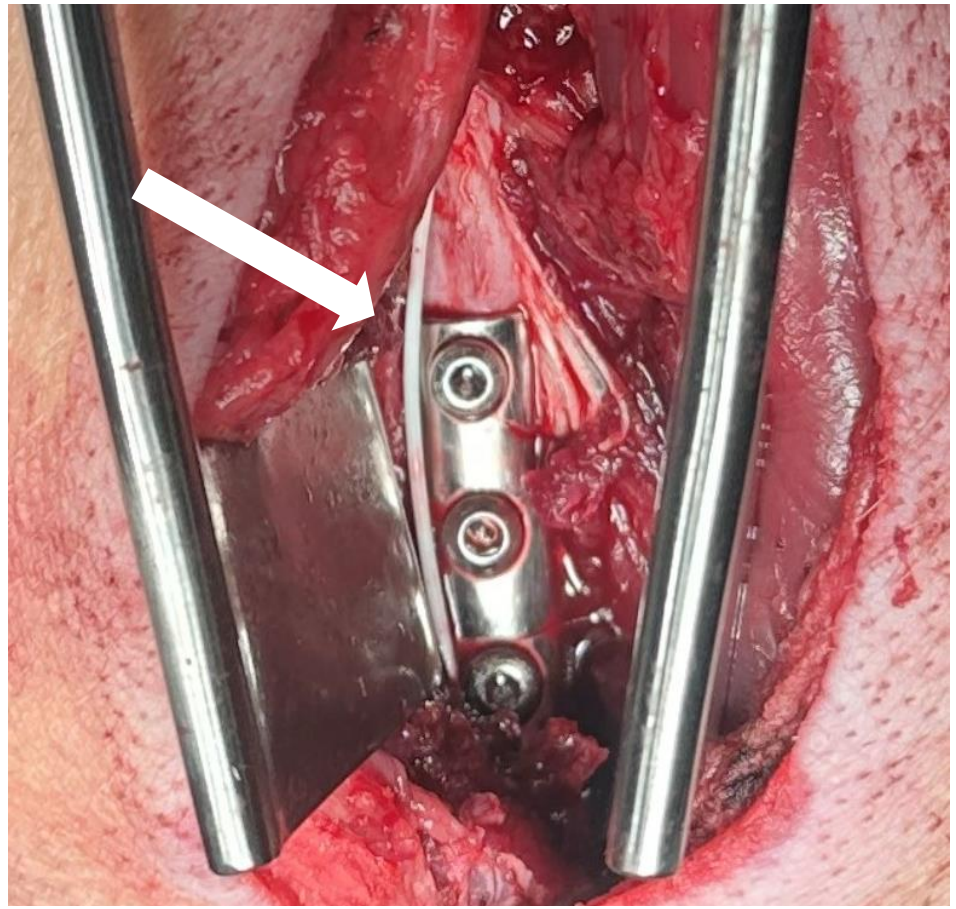
   This model supports development of field-deployable medical technologies for austere combat environments.

2. **Infection remained locally contained despite significant bioburden**

   No systemic acid–base, metabolic, or hematologic derangement was observed at 72 h despite significant local infection — suggesting an early window for intervention before systemic compromise.

3. **Biofilm formation on bone and hardware mirrors combat wound pathophysiology**

   Significant bacterial burden on both fibula bone and orthopaedic plate suggests biofilm formation, the primary target for local antimicrobial strategies.



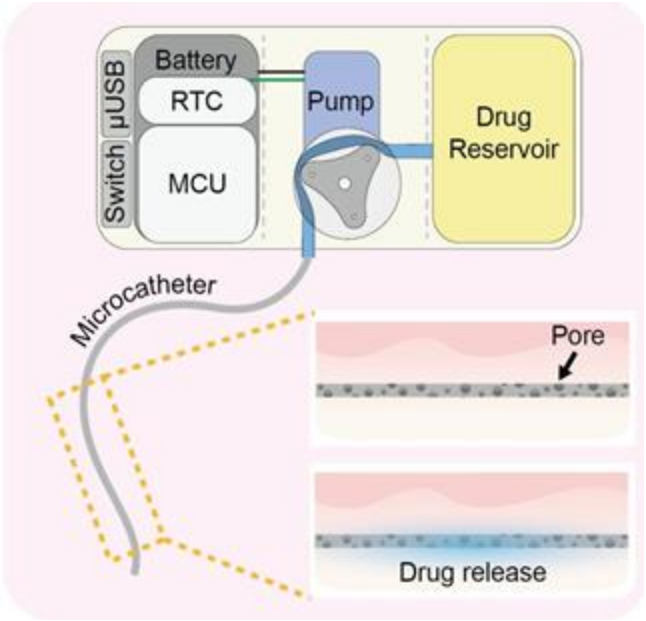
LIMITATIONS

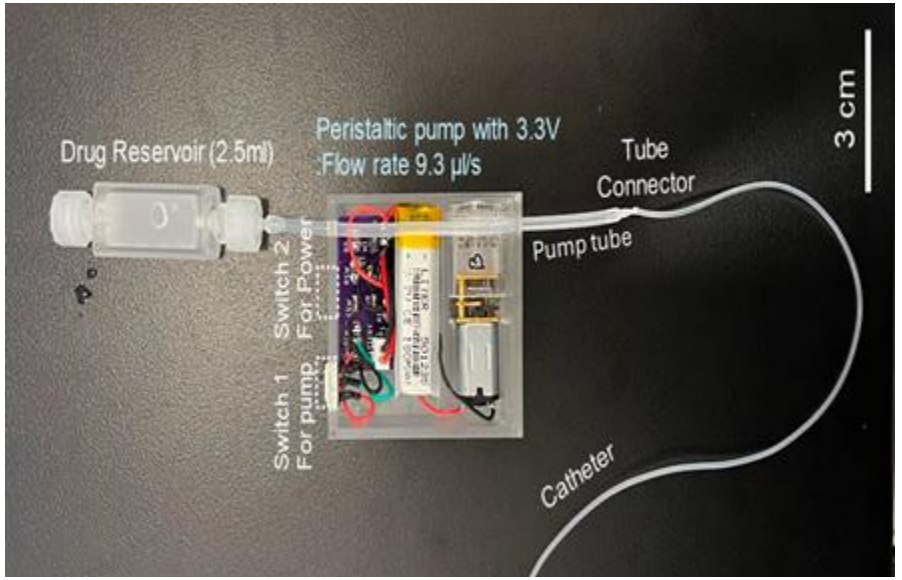
- Single pathogen (*K. pneumoniae*)
- Single time point (72 h) — later systemic response course not yet characterized
- Systemic panel limited to pH, lactate, and neutrophils — a broader biomarker panel could add sensitivity

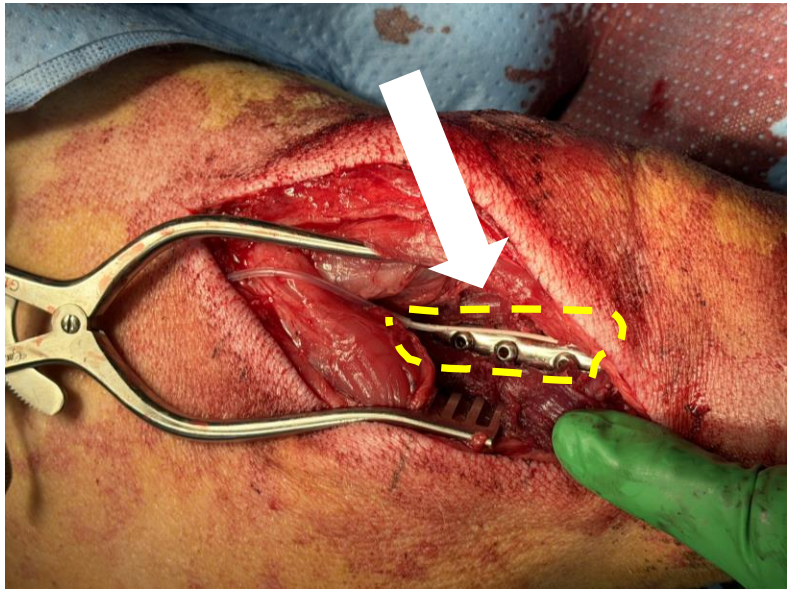
Next Steps

Using the validated FRI model to:

- ❑**Goal**: Discover a deployable local FRI countermeasure for settings where evacuation and surgical debridement are delayed.







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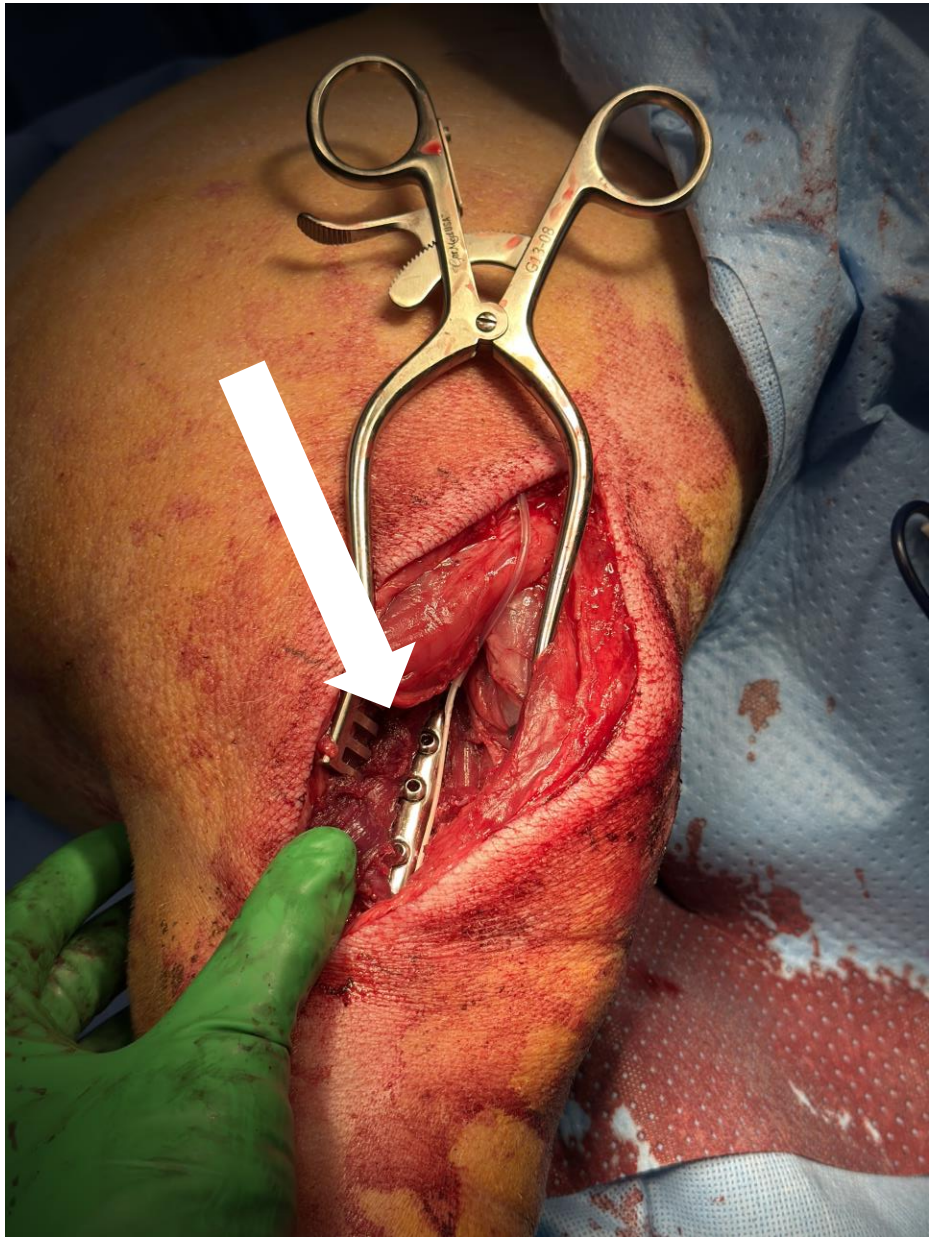

Questions & Discussion

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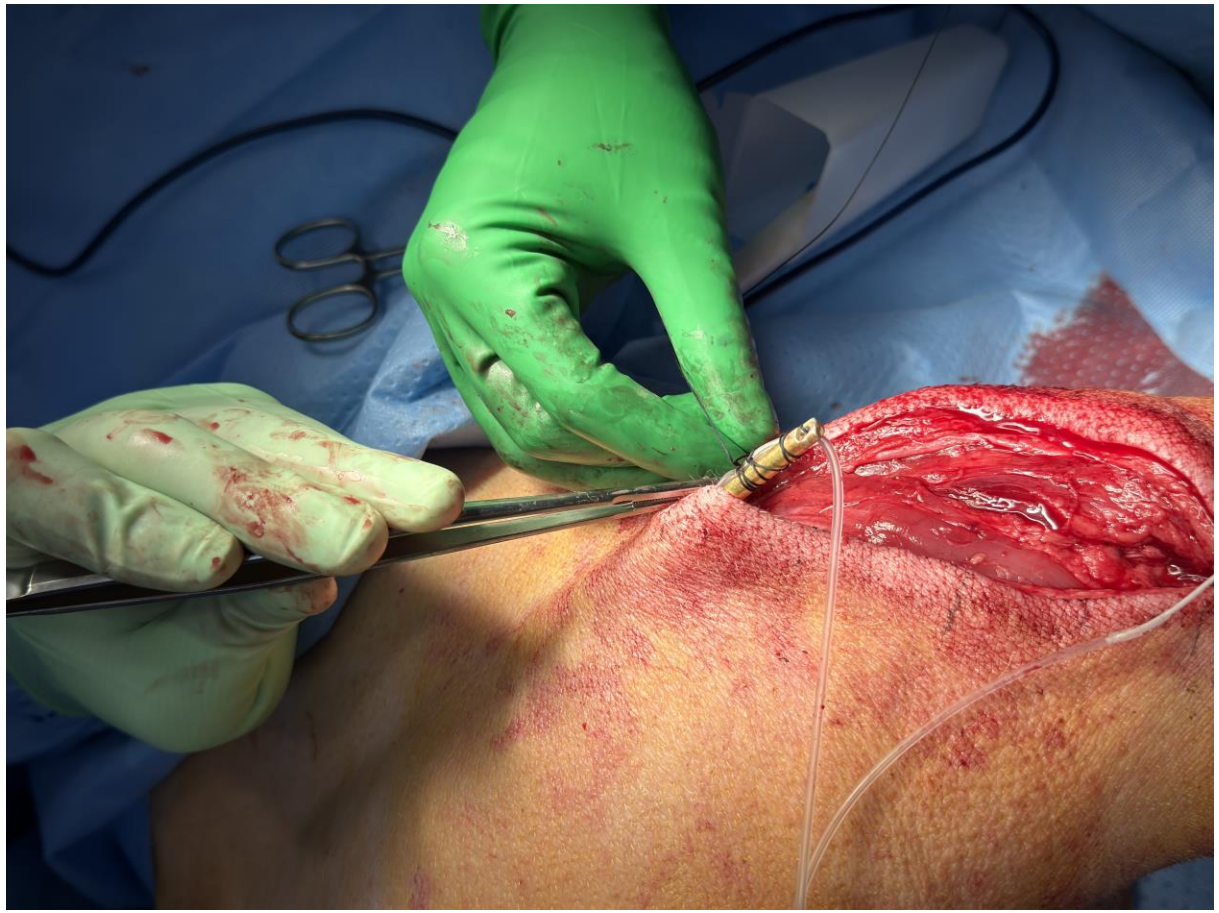
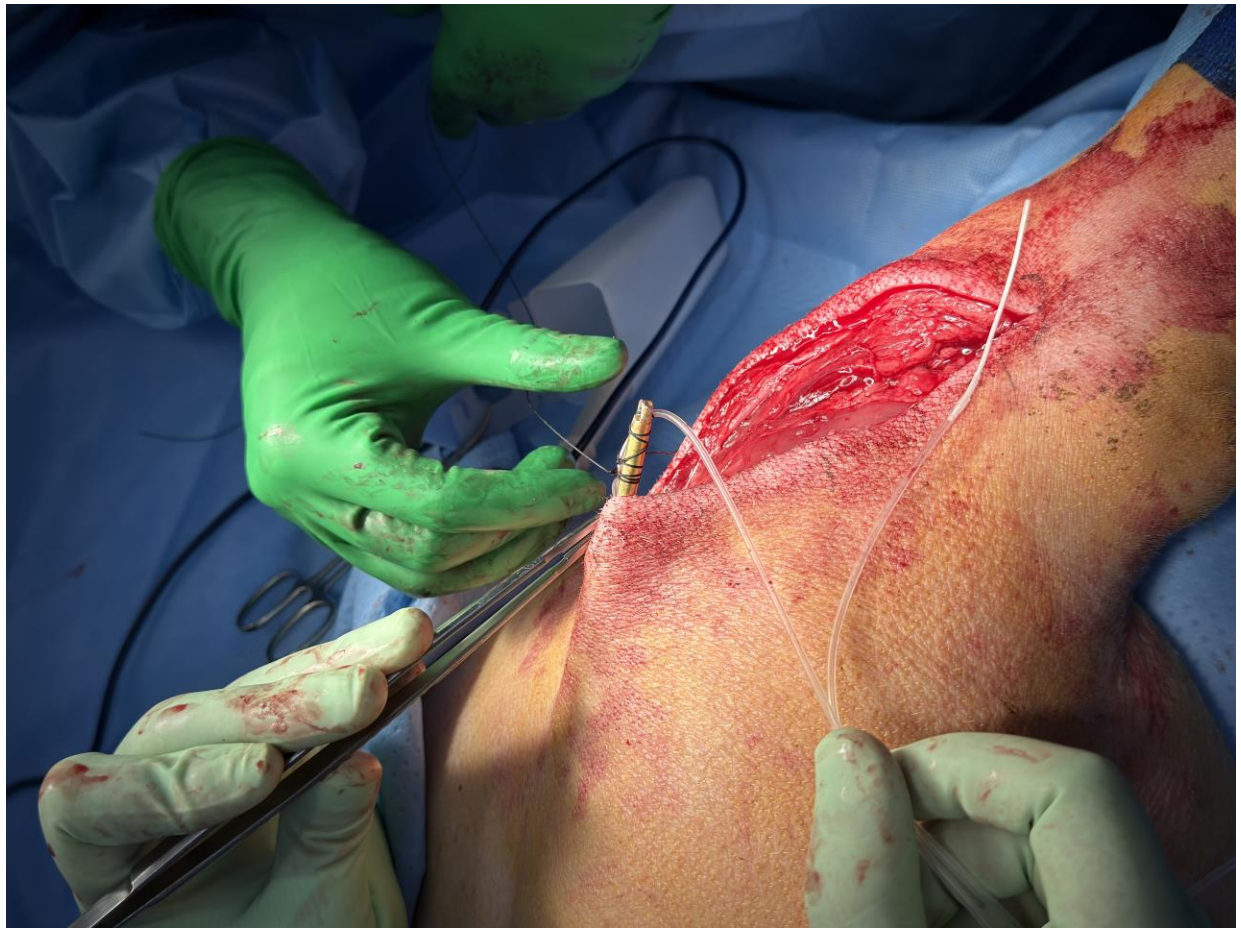
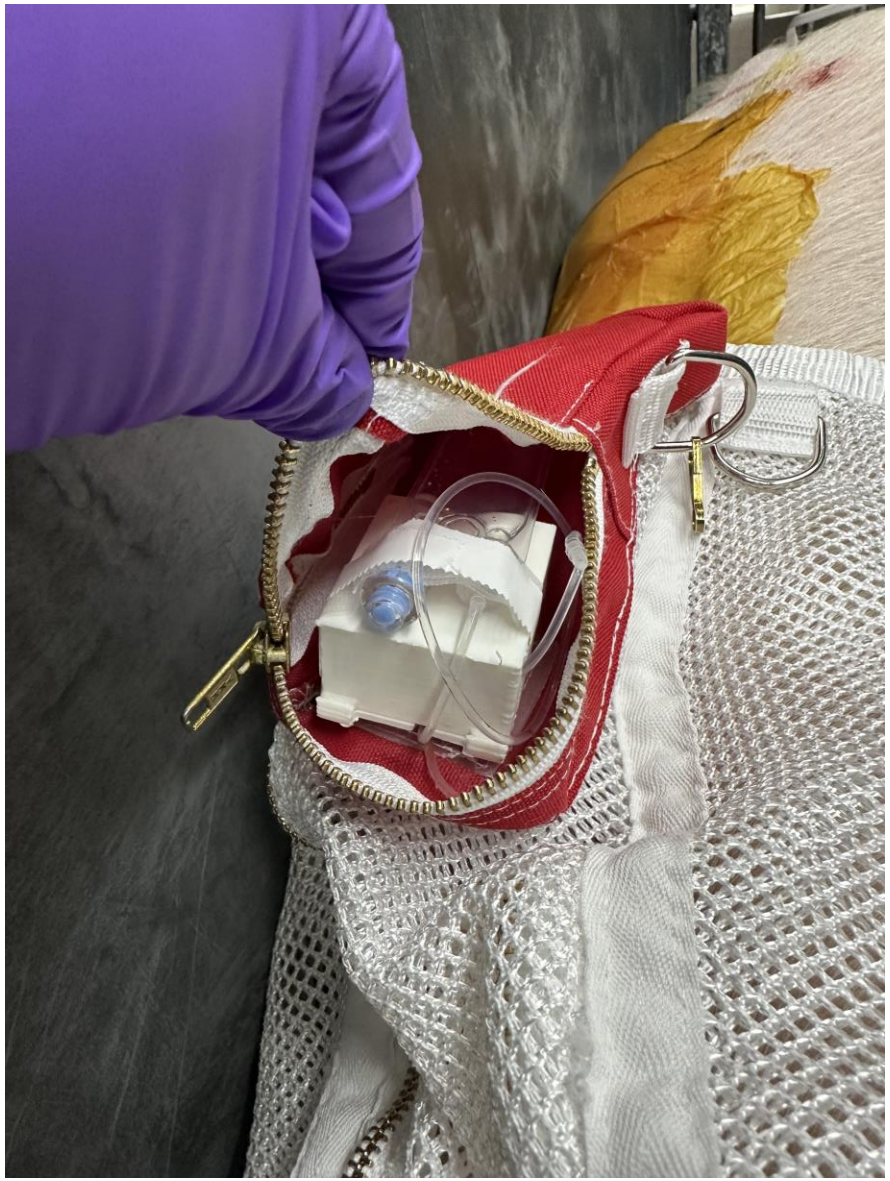
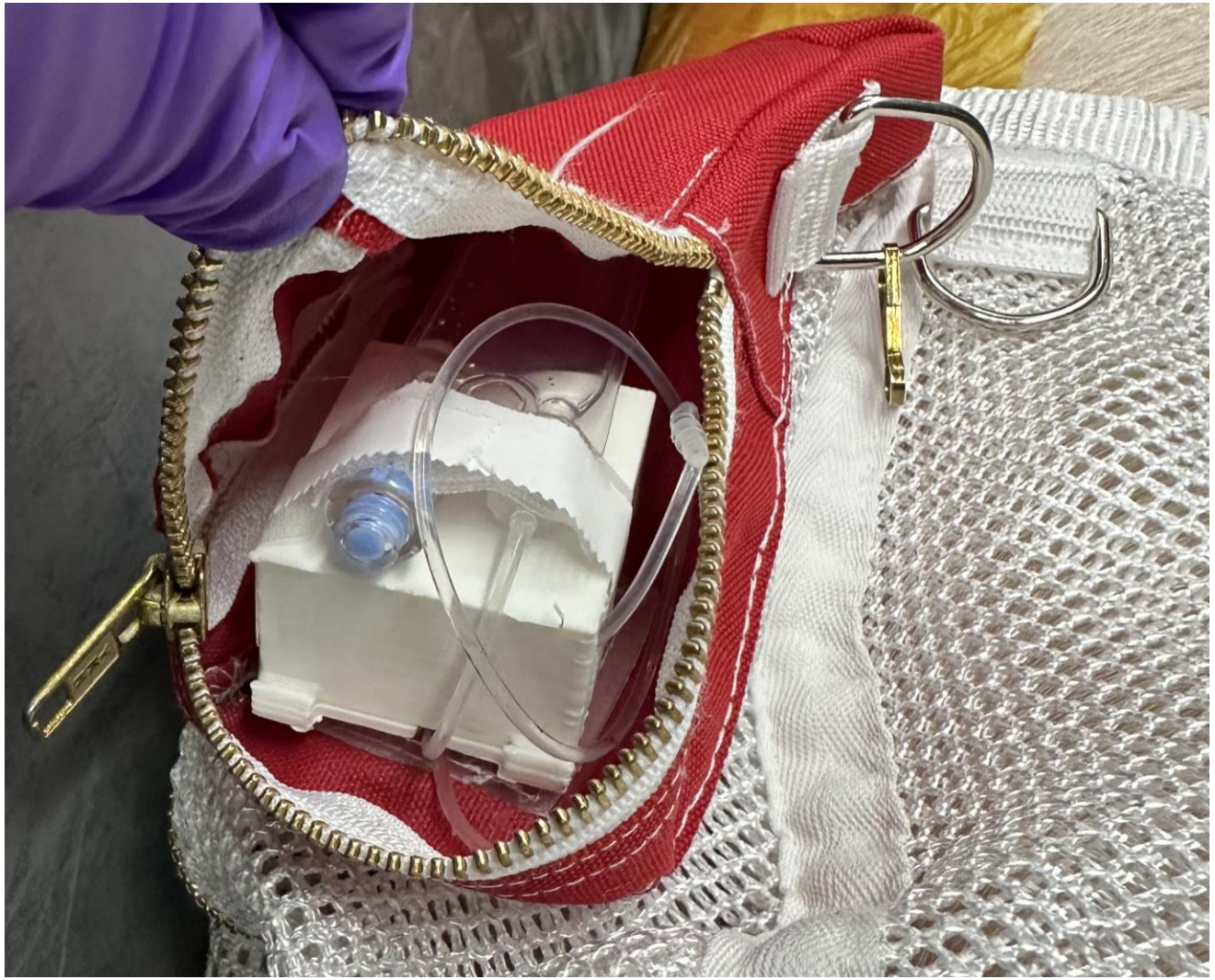
Tunneling through skin





The reservoir and pump placement





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