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Investigating Skin and Soft Tissue Infection (SSTI) mitigation using Far UV-C

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The Problem - Antibiotic dependence and resistance in Skin and Soft Tissue Injuries

- Antimicrobial resistant (AMR) infections are **rapidly increasing** and pose a threat to undo a century of medical progress
- **Alternative infection control methods** with broad spectrum effectiveness are desperately needed
- Surgical site infection (SSI) represent **20 % of hospital acquired infections** and patients are at **2-11 times higher risk of death**
- Wound infections require the highest uses of antimicrobial treatments, often due to poor infection control and are the **highest risk of death** beyond the immediate injury
- Antibiotic resistant bacteria, such as CRE (Carbapenem resistant Enterobacteriaceae) has become **resistant to nearly all antibiotics** we have today
- AMR infections threaten **increase the risk of mortality**, result in prolonged patient weakness and **elevate healthcare costs**

The Solution - Far UV-C xIP Infection Protection

- Using Far UV-C (200-235 nm) light to inactivate a broad spectrum of wound site pathogens and including antibiotic resistant bacteria
- Permits reduction in wound site pathogens **without contributing to further antibiotic resistance**
- Far-UVC light allows contactless disinfection which does not physically disrupt the wound site and can be used in conjunction with existing treatments for a **multi-layered approach**

Infections Per Year

Sepsis ***1.7M***
Surgery ***1.2M***
Chronic Conditions ***>30M***

Annual Deaths

> 35 000 in the US

Estimated Cost

> 4.6 B/year and growing

By 2050

1-10 Million Additional Deaths Globally

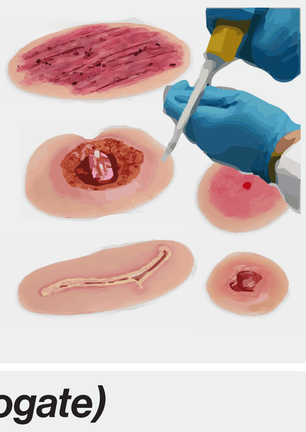
The Investigation - Mitigation in real world cases

- **Effectiveness** of different Far UV-C sources including broad spectrum and pulsed sources in reducing MSSA during in-vitro and ex-vivo studies
- Implications of occlusion on **real world wounds** for pathogen reduction
- **Penetration and scattering impacts from** expected fluids in wound sites
- Matching of **in-vitro and ex-vivo studies** to actual in-vivo studies carried out with consistent dosing and test methodology

Key Project Studies and Outcomes

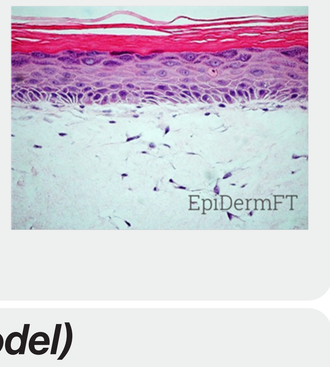
In-Vitro (Plate-Based assays)

- Pathogen selection and dose quantification
- UV exposure approach confirmation
- Dose response for each source
- Verifying fluence requirements for pathogens
- *Development of chemical dosimetry strategy**
- *Validation of fluorescence/luminance dose methods*[Y]*



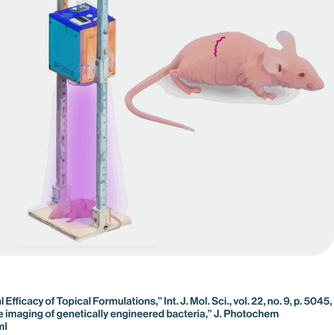
Ex-Vivo (Porcine skin)

- Porcine skin model[X]
- Development of wound formation approach
- Development of wound imaging techniques
- Pathogen viability studies performed via CFU
- *Validation of fluorescence/luminance dose methods**
- *Fluids and effects on fluence, dosimetry and pathogen response**



In-Silico Studies (Wound Modeling)

- Establishing theoretical requirements for effective pathogen reduction in wound
- Development of photogrammetry and optical modeling approach
- *Fluence modeled in complex wound geometries captured from assays**
- *Modeled occlusion and scattering in various fluids**



Ex-Vivo Assays (Human Surrogate)

- Human skin model using EpiDERM FT
- Validation of effective pathogen reduction for reporting via CFU
- *Measurement of cellular damage bio-markers (CPD formation)**
- *Validation of fluorescence/luminance dose methods**

In-Vivo Assays (Mouse Model)

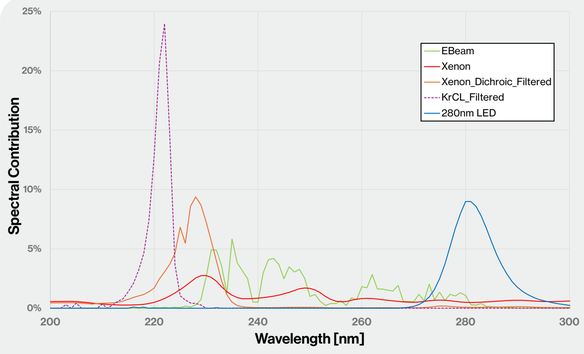
- Nude rodent model with humanized skin (SKH1 Elite)
- Live pathogen testing with MSSA or appropriate surrogate
- *Pathogen reduction characterized via CFU*
- *Longitudinal studies with fluorescent or bioluminescent cells showing UV dose**

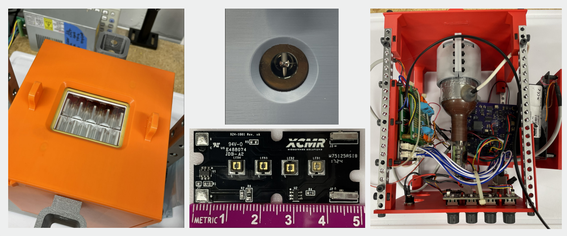
* Future Studies

X - M. Å. Andersson, L. B. Madsen, A. Schmidtchen, and M. Puthia, "Development of an Experimental Ex Vivo Wound Model to Evaluate Antimicrobial Efficacy of Topical Formulations," Int. J. Mol. Sci., vol. 22, no. 9, p. 5045,
Y - T. N. Demidova, F. Gad, T. Zahra, K. P. Francis, and M. R. Hamblin, "Monitoring photodynamic therapy of localized infections by bioluminescence imaging of genetically engineered bacteria," J. Photochem
Z -"Ivis Optical Imager," THE OLIVE LABORATORY. Accessed: Apr. 12, 2024. [Online]. Available: https://www.OliveLab.org/ivis-optical-imager.html

Project Work Completed / In-Progress

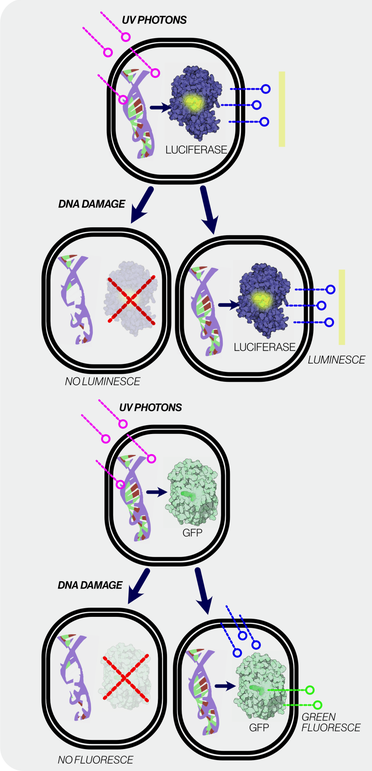
UV-C Sources Studied

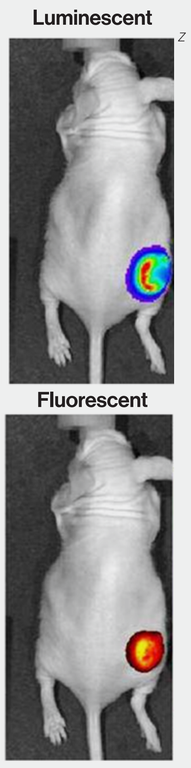




- Range of sources used in the study including:
  - KrCl Excimer (222nm peak)
  - Electron Beam Cathodoluminescent (235nm peak)
  - Pulsed Xenon (230nm peak)
  - 280nm LED (280nm peak)
- Includes both pulsed, multi-spectrum sources (EBeam CL and Xenon) and continuous narrow spectrum sources (KrCL and LED)
- Only currently available commercial or high TLR sources used in the study
- Equivalent dose and equivalent ACIGH TLV limit (skin) optical outputs used as limits of study

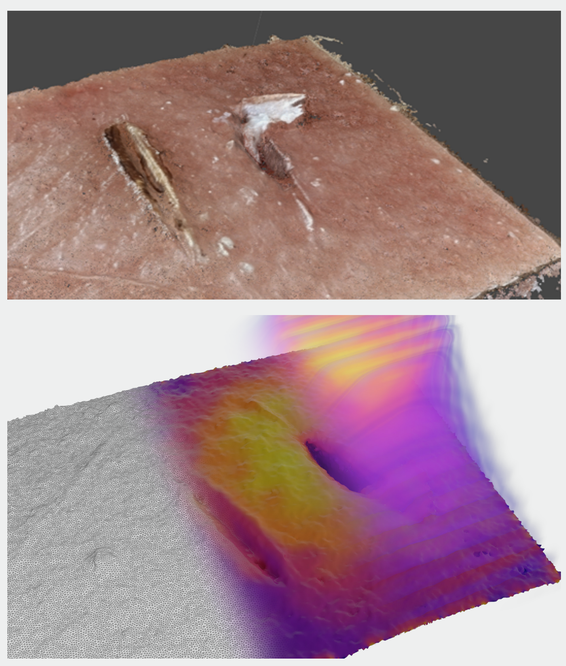
Temporal Dose Estimation





- Studies using engineered MSSA strains which either luminescent or fluorescent reporters
- Viable cells will continue to luminesce/fluoresce giving indication of successful gene expression
- Testing with reporters underway to understand UV-C response:
  - Establishment of best process (luminescent or fluorescent)
  - Demonstration of quenching / decay rate under UV-C exposure and control plates
  - Establishment of dose response versus luminescence/fluorescence of the strains versus CFU
  - Repeatability and ex-vivo suitability/performance studies
- Potential imaging with IVIS as part of in-vivo assays to determine spatial distribution of inactivation

Wound Modeling



- Wounds created to mimic multiple injury types and sizes for ex-vivo (Porcine) studies
- Actual wound geometry results in occlusion, scattering and altered penetration compared to plate assays
- In-silico studies are used to determine best approach including:
  - Source view angle and view factor
  - Traversal/multiple exposure requirements
- 3D geometry for created wounds will be created for simulation using macro photogrammetry
  - Multiple images taken of wound site at different distance and angles
  - Depth estimation and point clouds from images
  - Re-triangulation of point cloud to determine geometry
- Geometry can be used directly for in-silico experiments