# OPTIMIZATION OF ADHESIVE, 3D-PRINTED HYDROGEL PATCHES AS A DRUG DELIVERY SYSTEM FOR WOUND HEALING

Srilekha Venkatraman[1], Emma Etter[1], Juliane Nguyen[2]

[1]Joint Department of Biomedical Engineering at UNC Chapel Hill and NC State; [2]UNC Eshelman School of Pharmacy Division of Pharmacoengineering and Molecular Pharmaceutics

PAdH patches are resistant to degradation and exhibit sustained release of wound healing proteins.
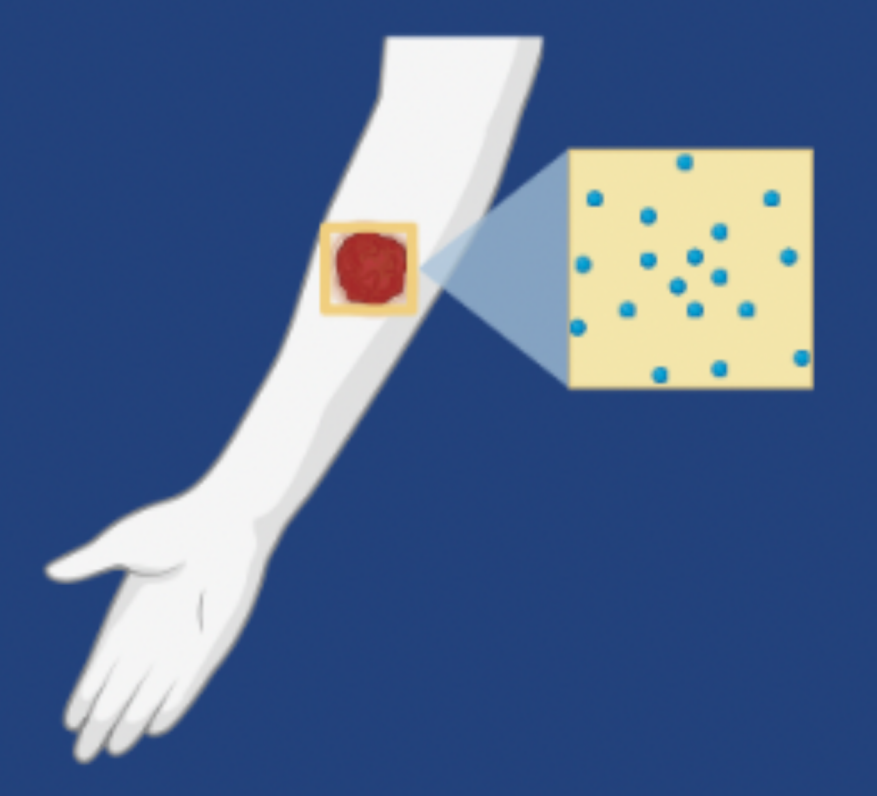
BACKGROUND

INTRODUCTION:
- >2.5 million people affected by chronic wounds in the US annually
- Current growth factor treatments targetting complications in angiogenesis have low bioavailability

PROPOSAL: Protein-delivering, adhesive, hydrogel patches (PAdH) patches for the delivery of therapeutic protein (PDGF) to facilitate wound healing

**PURPOSE:** Optimize PAdH patch composition for delivery of therapeutic proteins

OBJECTIVES:
Protein loading and release efficiency
- Maximize amount of protein loaded into crosslinked ink
- Sustain the release of protein from the patch
- Ensure appropriate rate of release of PDGF for accurate dosing of therapeutic
Degradation of PAdH patches in collagenase
- Fabricate patches for resistance to degradation in physiological levels of collagenase
  - Gelatin is derived from collagenase, which is broken down by collagen
- Establish longevity of patch for use in long-term wound treatment

METHODS

PATCH COMPOSITION AND PRINTING:
- Gelatin methacrylate-based (GelMA)
- Square patch; photocrosslinked with UV light in 3D printer
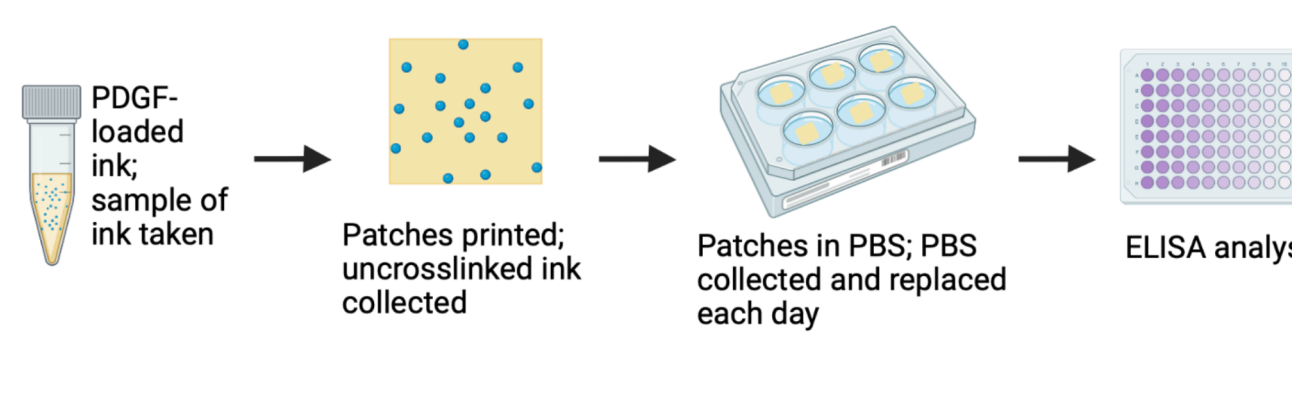
Digital light processing
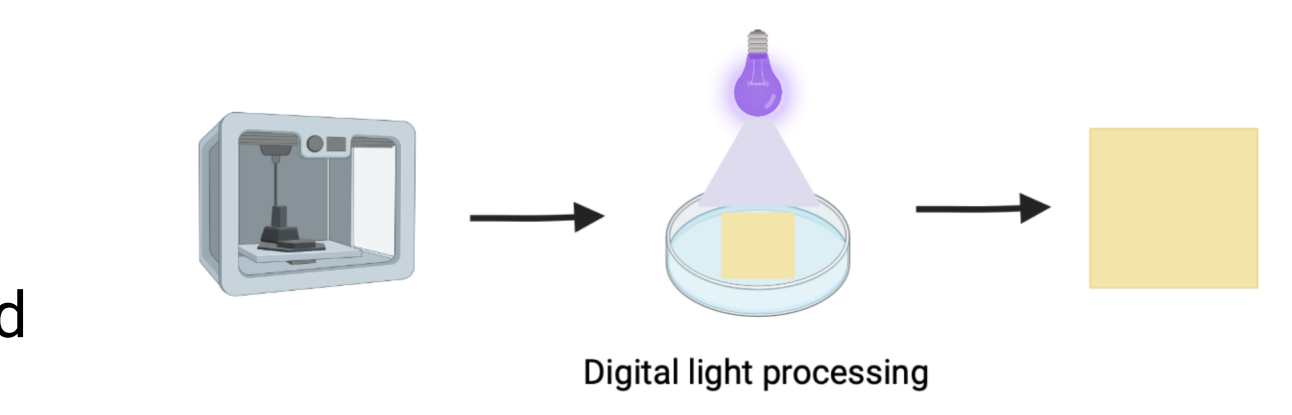
PROTEIN RELEASE:
- Ink loaded with PDGF
- Patch put in PBS solution
- PBS solution obtained and changed over a series of days
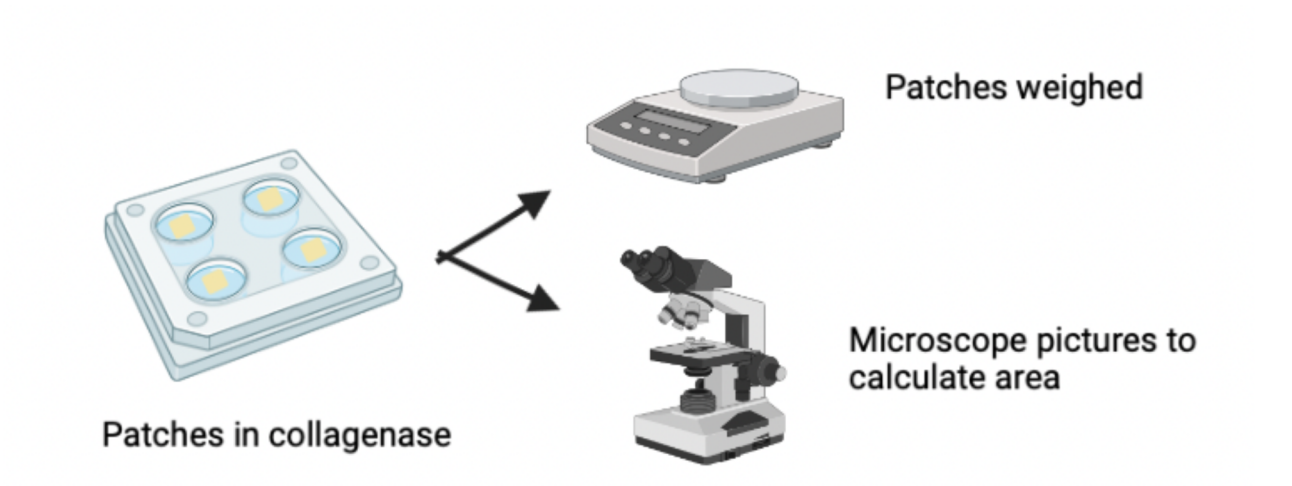- ELISA conducted on supernatants

GFP-loaded ink crosslinked • Patches homogenized • ELISA analysis
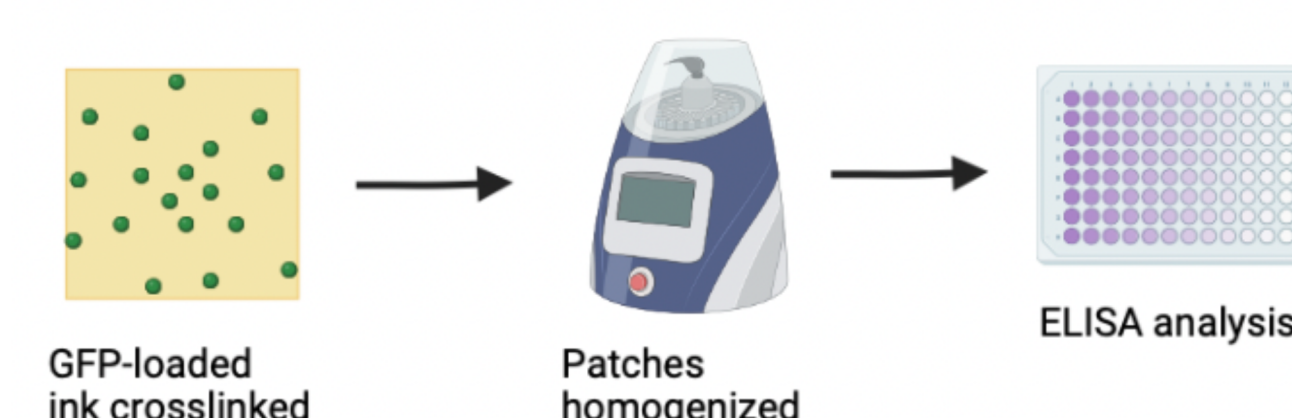
PROTEIN LOADING:
- Print patches loaded with green fluorescent protein (GFP)
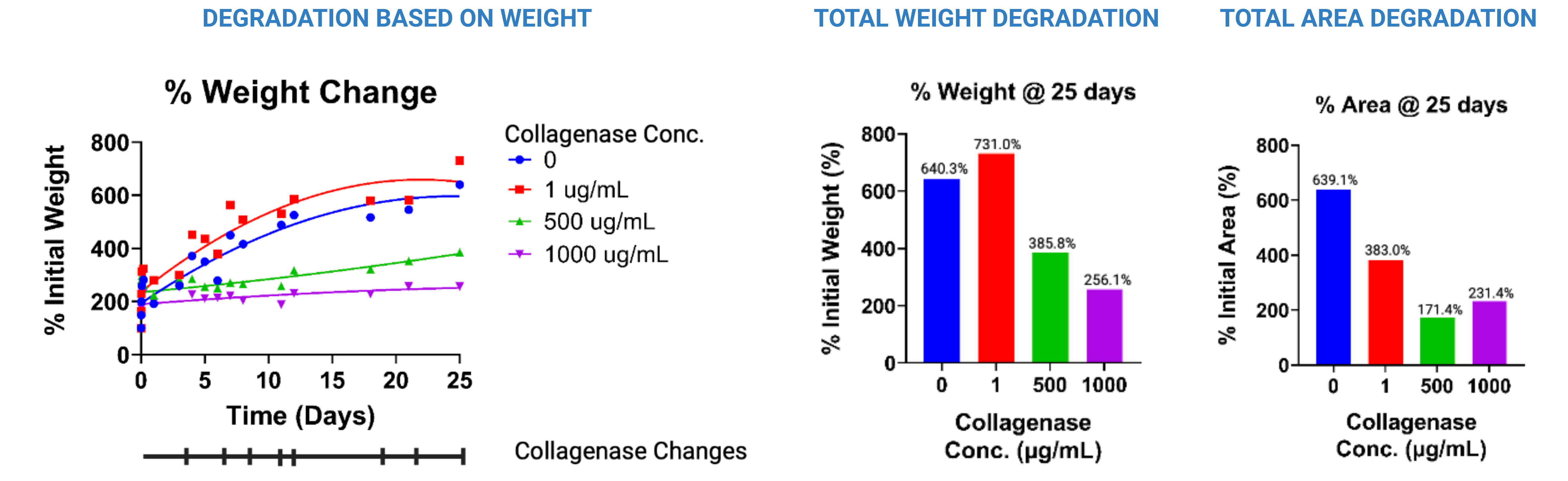- Patches homogenized and analyzed with ELISA

PDGF-loaded ink, sample of ink taken • Patches printed; uncrosslinked ink collected • Patches in PBS; PBS collected and replaced each day • ELISA analysis

PATCH DEGRADATION:
- Patches put in collagenase solutions
- Patch weights and areas recorded over a series of days

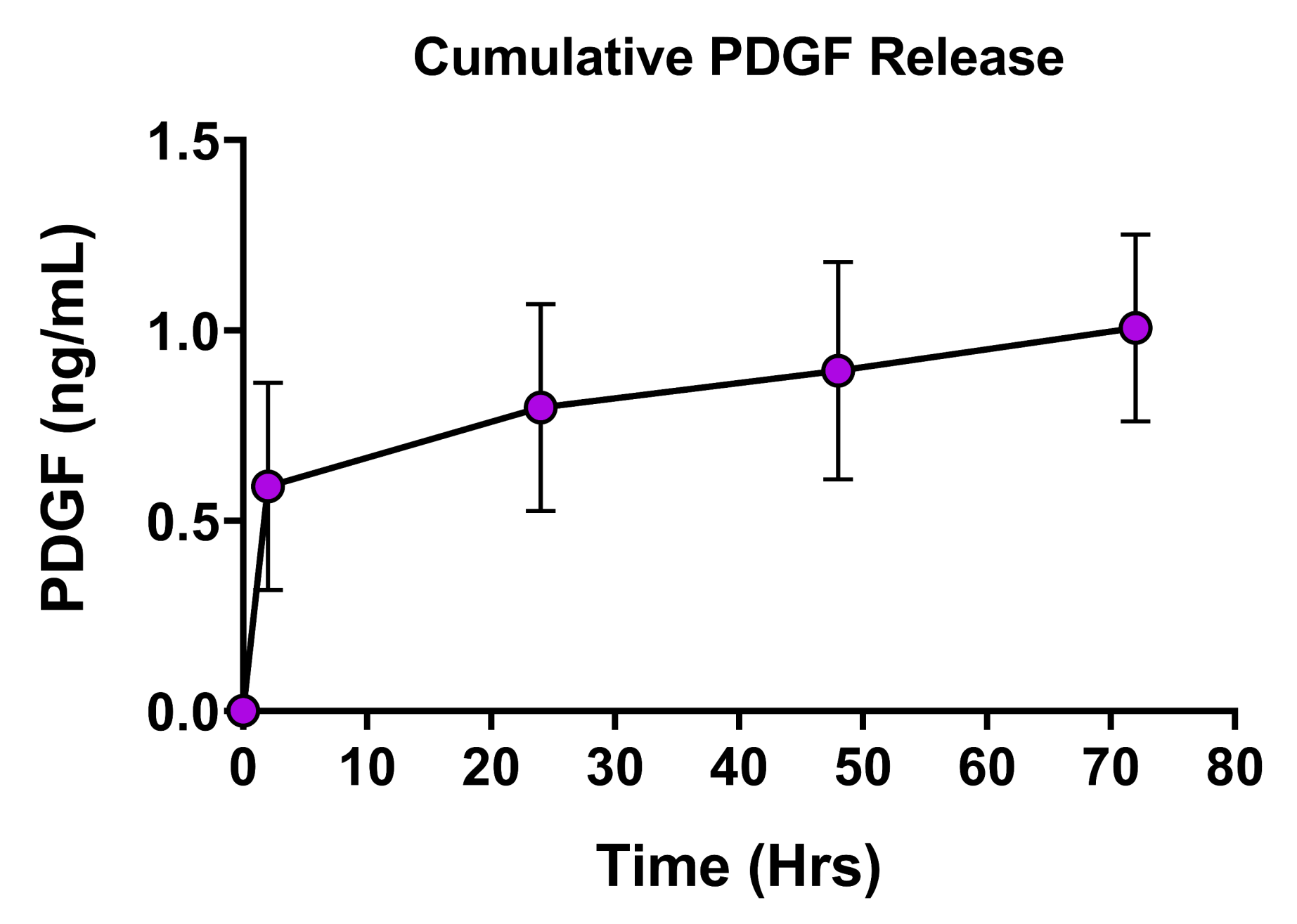Patches weighed • Patches in collagenase • Microscope pictures to calculate area

RESULTS - PROTEIN LOADING AND RELEASE

Cumulative PDGF Release

There is sustained release of PDGF from patches over time for 3 days.

Percent GFP Loaded

- 100 ng: 79.1%
- 250 ng: 78.5%
- 500 ng: 76.9%
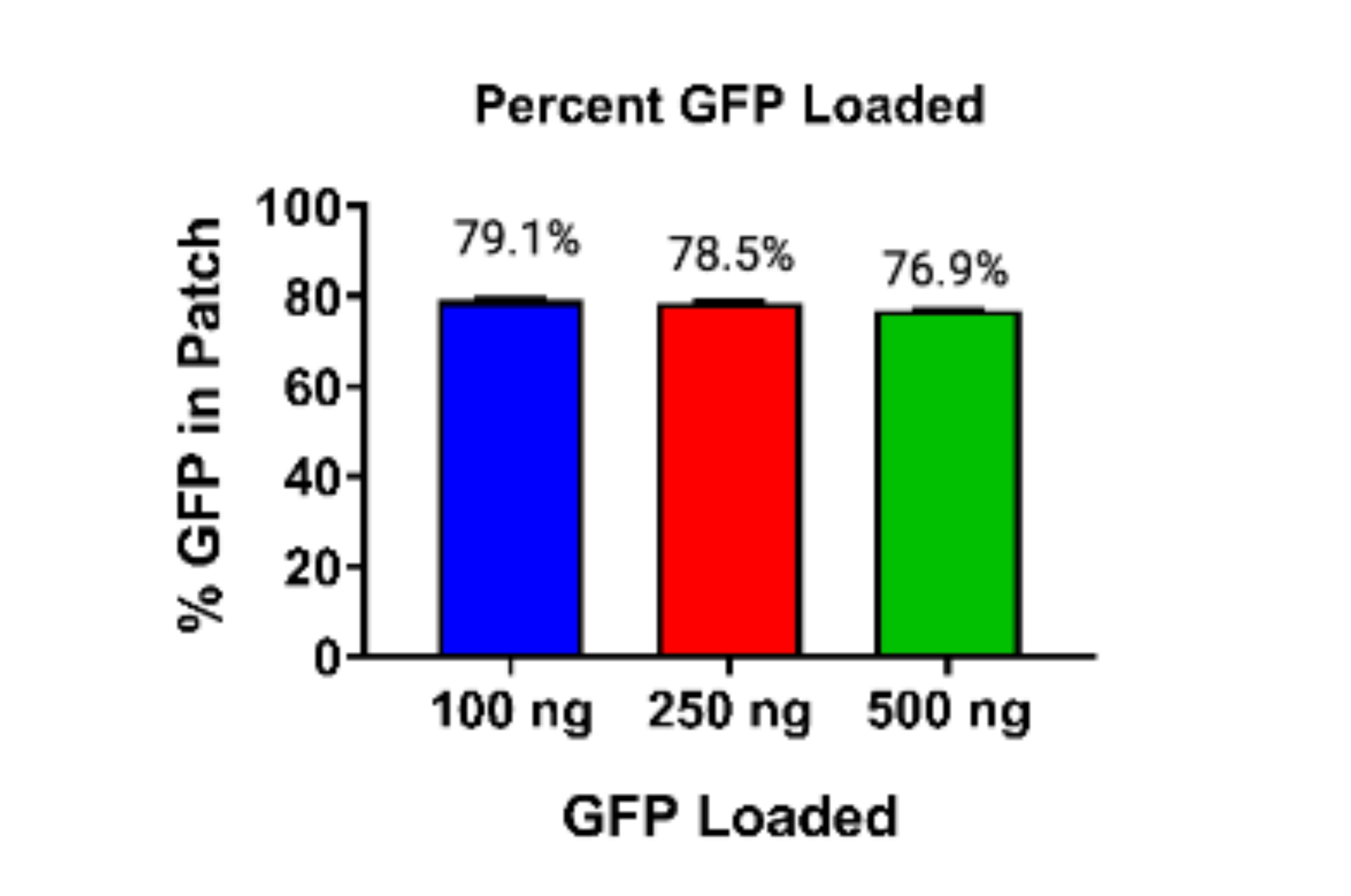
The concentration of GFP loaded into the ink does not affect the amount present in the patch

Bioink under light → Some ink (containing GFP) remains uncrosslinked / Remaining GFP in crosslinked ink

$$\% \text{ GFP Loaded} = 100 - 100 \left(\frac{\text{amount in uncrosslinked ink}}{\text{total GFP loaded}} \right)$$

RESULTS - PATCH DEGRADATION

DEGRADATION BASED ON WEIGHT

% Weight Change

Collagenase Conc.
- 0
- 1 ug/mL
- 500 ug/mL
- 1000 ug/mL

Collagenase Changes

PAdH patches undergo less degradation in physiological levels of collagenase

TOTAL WEIGHT DEGRADATION

% Weight @ 25 days

- 0: 640.3%
- 1: 731.0%
- 500: 385.8%
- 1000: 256.1%

Collagenase Conc. (µg/mL)

PAdH patches in physiological levels of collagenase swell similarly to patches in water.

TOTAL AREA DEGRADATION

% Area @ 25 days

- 0: 639.1%
- 1: 383.0%
- 500: 171.4%
- 1000: 231.4%

Collagenase Conc. (µg/mL)

PAdH patches are more resistant to area decrease in physiological levels of collagenase

DEGRADATION BASED ON AREA

% Area Change

Collagenase Conc.
- 0
- 1 ug/mL
- 500 ug/mL
- 1000 ug/mL

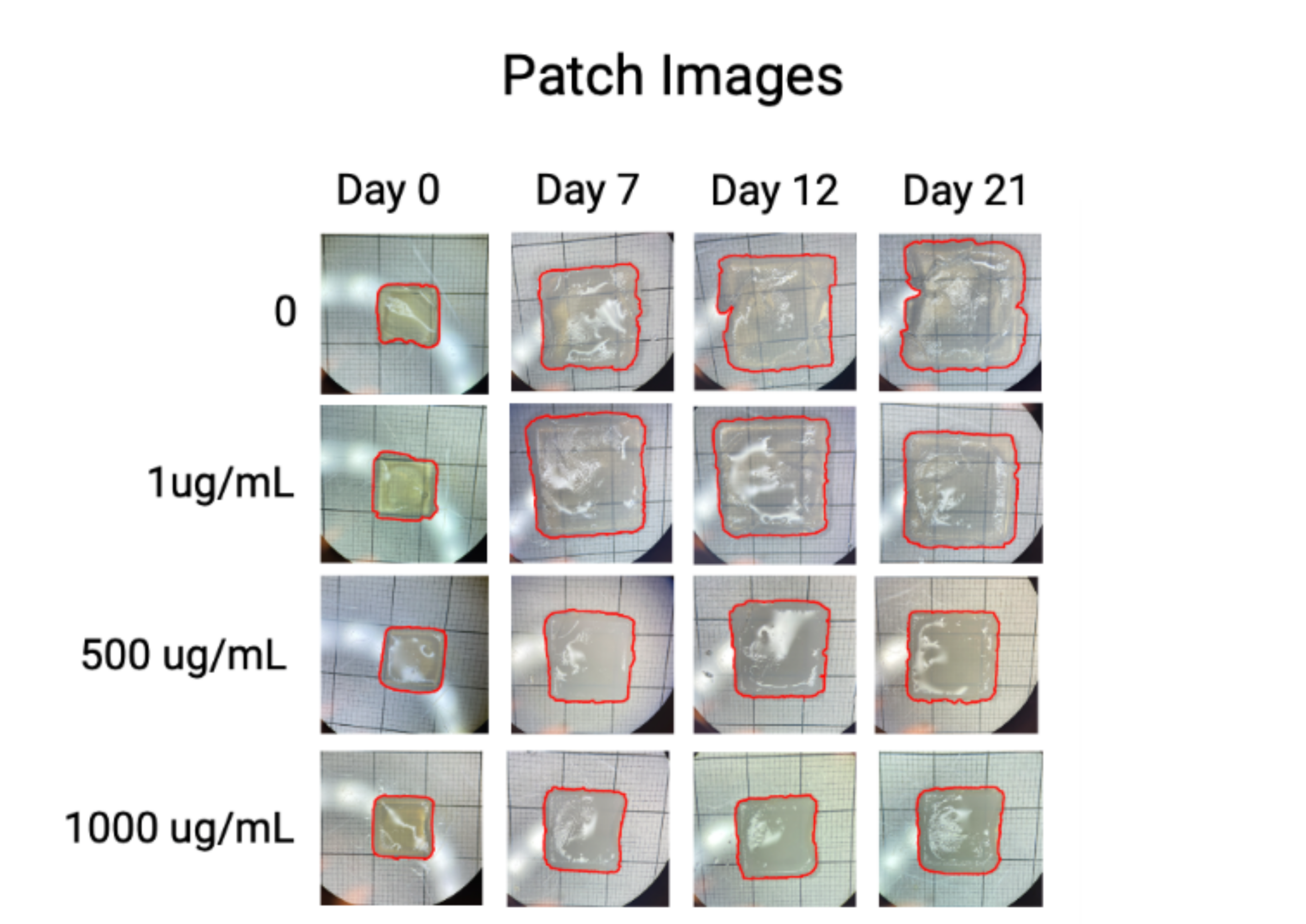Collagenase Changes
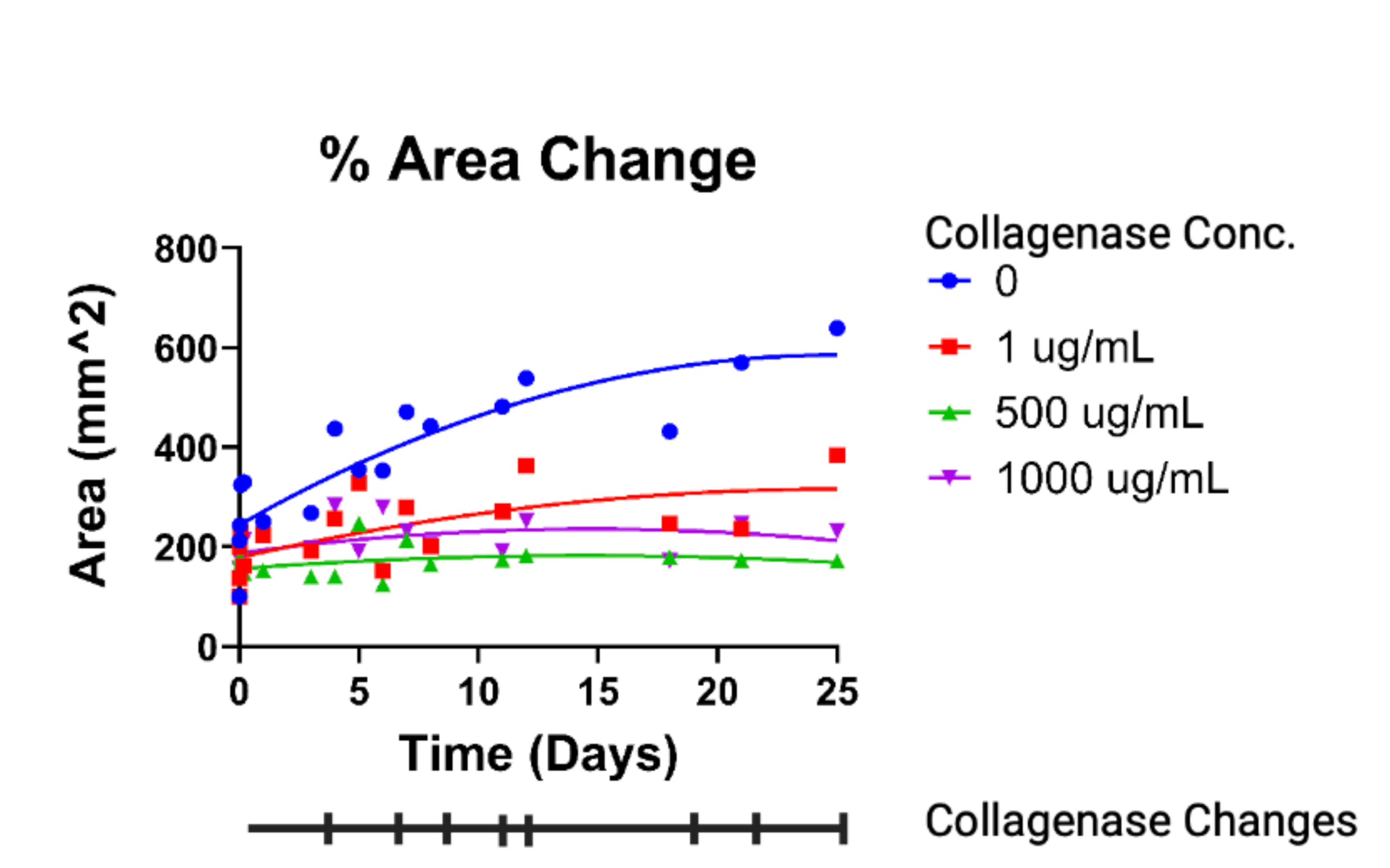
Physiological levels of collagenase facilitate patch swelling and resistance to degradation.

IMAGES OF PATCH DEGRADATION

Patch Images

Day 0, Day 7, Day 12, Day 21 (rows: 0, 1ug/mL, 500 ug/mL, 1000 ug/mL)

PAdH patches in physiological levels of collagenase exhibit similar swelling to patches in no collagenase.

CONCLUSION

DISCUSSION:
- PAdH patches are resistant to degradation in physiological levels of collagenase for 25 days
- GFP successfully loaded into PAdH patches at 78% efficiency
- Observed sustained release of PDGF from PAdH patches for 3 days

FUTURE DIRECTIONS:
- Further optimize protein release
  - Investigate potential for controlled release of PDGF
- Introduce engineered yeast (*S. cerevisiae*) as a drug delivery agent to secrete PDGF
  - Load yeast into patches
  - Test loading and release efficiency of PDGF with yeast delivery
  - Observe patch degradation with loaded yeast

Joint Department of **BIOMEDICAL ENGINEERING** | UNC CHAPEL HILL | NC STATE UNIVERSITY

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