Development of a Human Model for In-Water Chemical Absorption

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NON-DISCLOSURE

Caroline Smith has no conflicts to report.

INTRODUCTION

Military divers frequently operate in contaminated water environments

- Potential exposure to chemical toxicants during underwater missions.
- Health risks remain poorly characterized.

Current in-water chemical safety guidance is limited

- Airborne inhalation and dermal exposure (OSHA) and drinking-water (EPA) based guidance is available, but **in-water dermal absorption guidance does not exist**.
- Existing in-water dermal absorption recommendations are based largely on expert opinion.
- ***Lack of empirical human data to support risk assessment.***

RATIONALE

No Established Exposure Limits For Dermal Absorption Of Chemical Toxicants During In-water Operations

Need for research

1. **Develop an in-water dermal chemical absorption model in humans** ➞
2. Quantify in-water dermal chemical exposure limits ➞
3. Generate data to inform exposure-risk relationships.

Research Impact

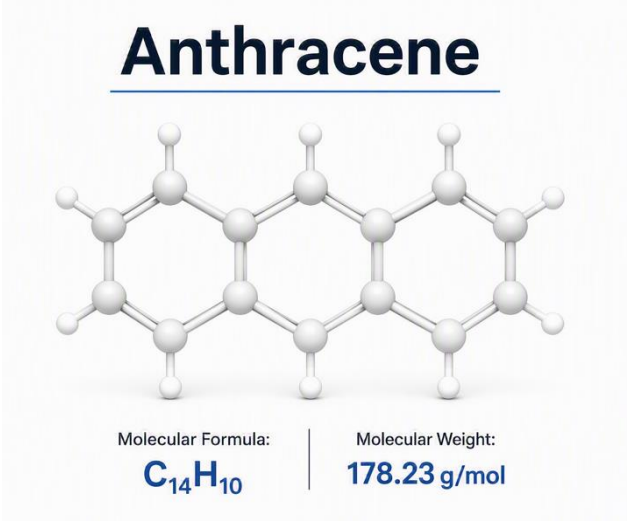
- Support development of evidence-based health and safety guidelines.
- Improve risk management for military diving operations.
- Enhance protection of diver health and operational readiness.

PURPOSE

Develop a safe and effective method for evaluating whole-body in-water dermal chemical absorption in humans.

METHODS

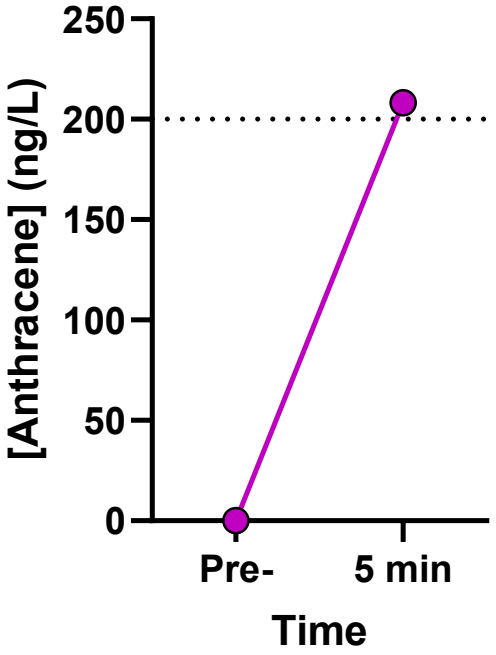
- Polycyclic aromatic hydrocarbons (PAHs) are common in coastal waters due to incomplete fossil fuel combustion.
- **Anthracene** (**Anth**) is a non-toxic, non-carcinogenic three-ring PAH that is readily dissolved in surface waters.
- Anth concentration of **200 ng/L** was chosen because:
  a) It is within safe drinking-water limits; and
  b) It is approximately the OSHA limit for airborne dermal and inhalation exposure.
  c) Precedent in human subjects experimental settings.



METHODS: ANTHRACENE SOLUTION DEVELOPMENT

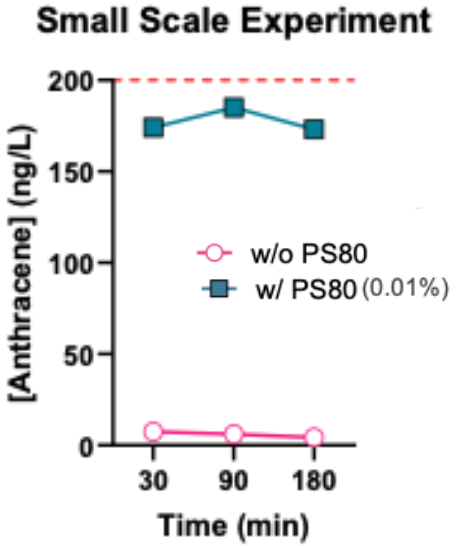
Anthracene is hydrophobic (solubility limit 0.044 mg/L at 25°C)

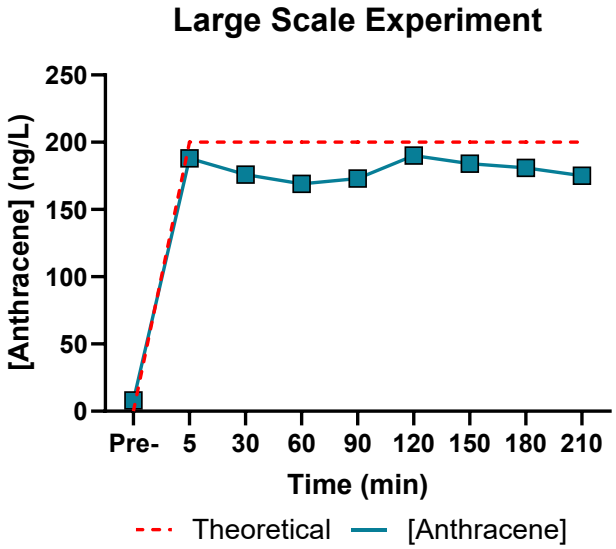
- **Target concentration = 200 ng/L** (well below solubility limit)
- Add 0.0782 mg to 391 L of water
  - *Difficult to accurately measure.*
- Create stock solution of volatile solution (e.g., methanol) with high anthracene solubility.
- Add volume of stock solution to tub and let the methanol evaporate with slow mixing.



METHODS: ANTHRACENE SOLUTION DEVELOPMENT

Polysorbate 80 (PS80): *Surfactant, solubilizer. Common in foods, pharmaceuticals and beauty products.*





EXPERIMENTAL MODEL

Randomized, double blind design

4h Head out immersion

- *Urine collected hourly*
- *Participants drank (Gatorade Zero) to replace*

'Contaminated' water:

200 ng/L anthracene
+
0.01% Polysorbate 80

Salinity 30 ppt, 35°C

Control immersion:

0.01% Polysorbate 80 only

Salinity 30 ppt, 35°C

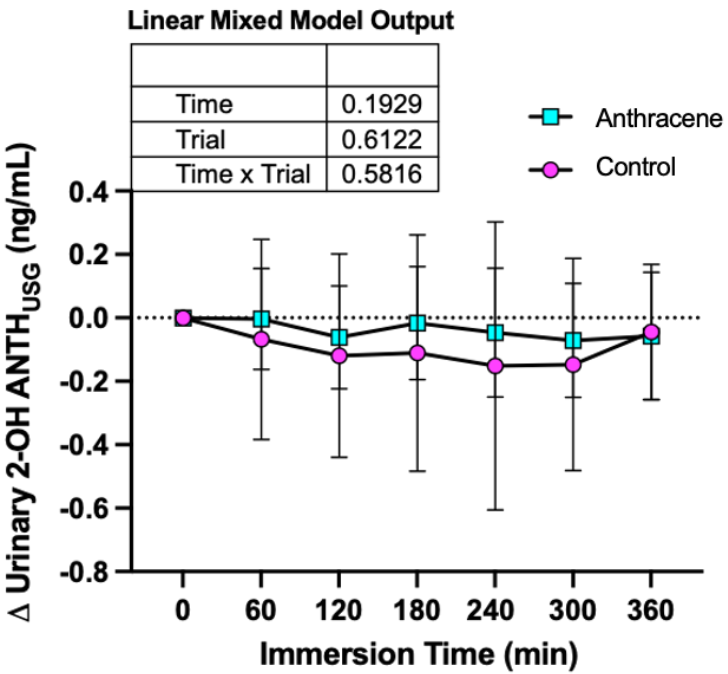
Primary outcome variable:

urinary 2-OH-anth

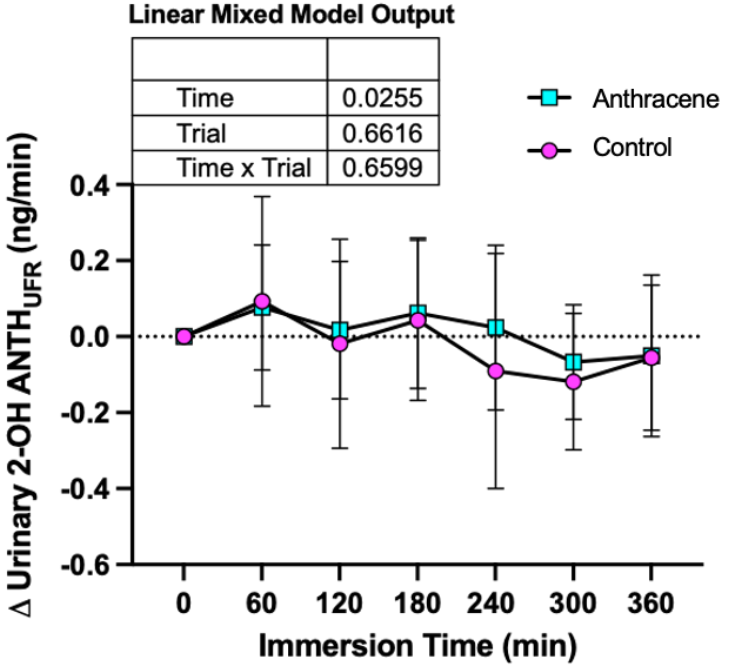
(corrected to specific gravity and urine flow rate)

RESULTS

Urine specific gravity normalized



Urine flow rate normalized

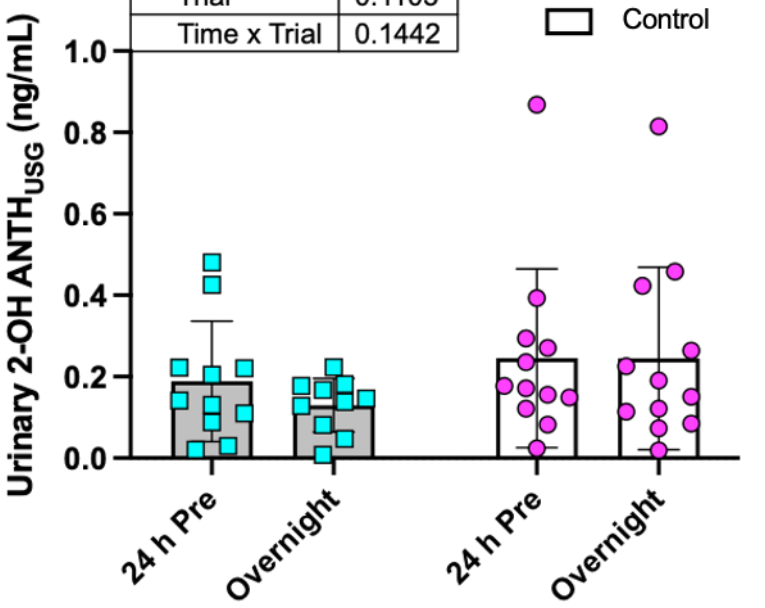


n=11, mean ± SD

RESULTS

Linear Mixed Model Output

Time	0.3493
Trial	0.1103
Time x Trial	0.1442



n=11, mean ± SD

Conclusion:

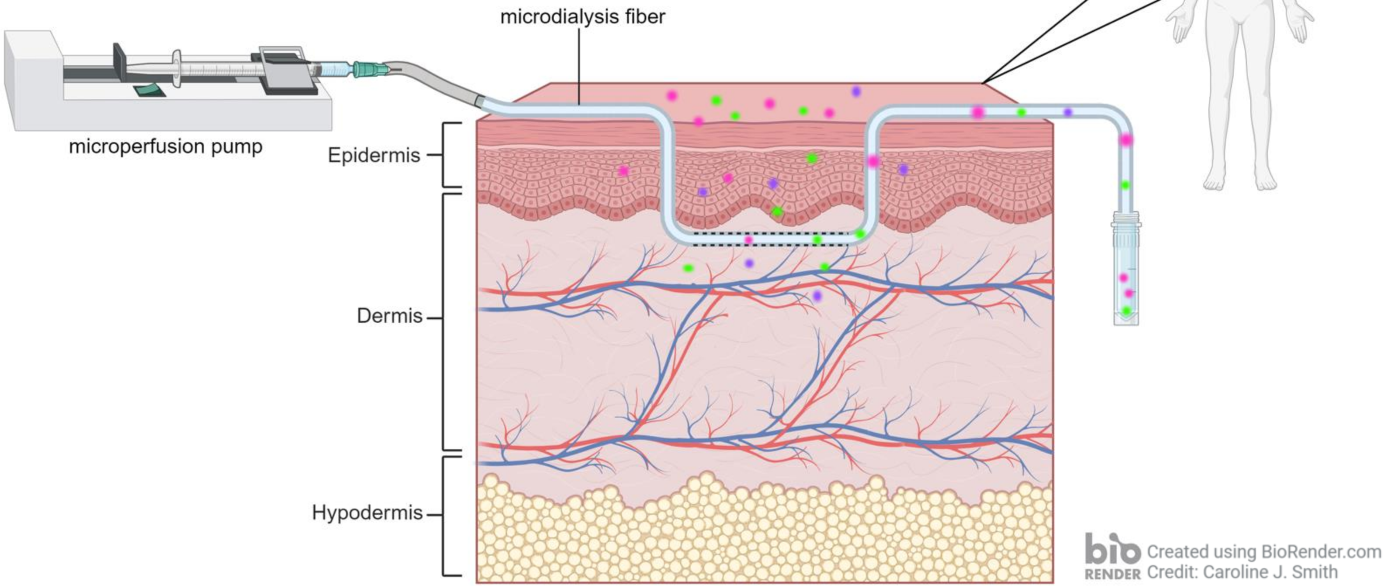
Anthracene concentration in water is too low to reliably detect increases in urinary 2-OH-Anth.

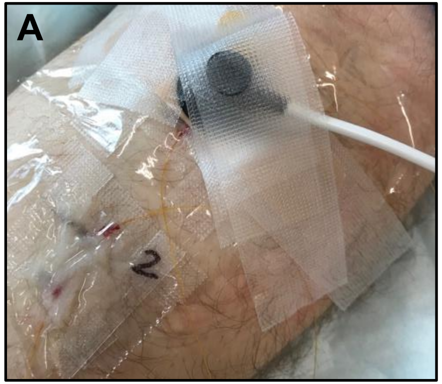
Model Development Options:

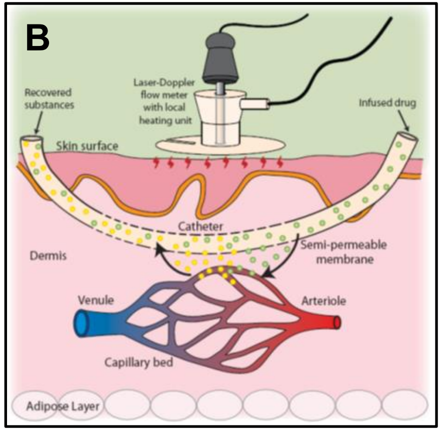
1) Increase anthracene concentration (ethical considerations)
2) **Consider alternative models.**

LOCALIZED DERMAL ABSORPTION

Intradermal Microdialysis







Kenney, WL. J Appl Physiol 123(5):1024–1038, 2017

LOCALIZED DERMAL ABSORPTION

Intradermal Microdialysis

**Anthracene administered in Aquaphor*

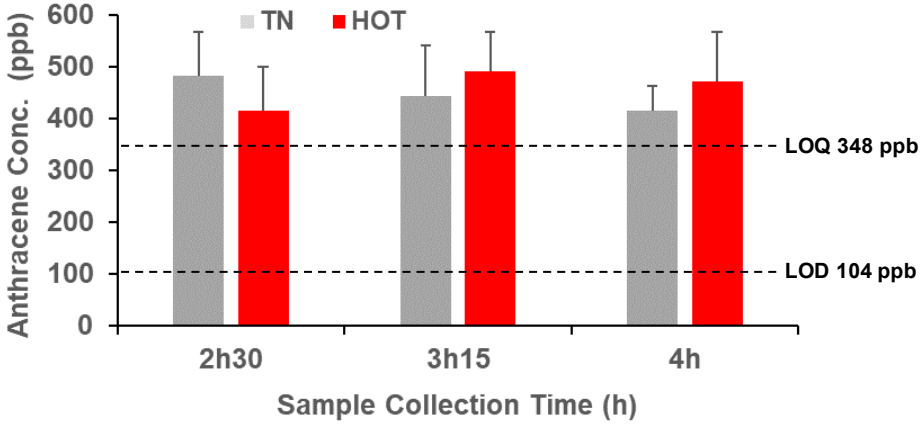


Figure 1. Anthracene dialysate concentration (ppb) over time. n=8 (5 Male, 3 female).

*Interaction (site*time), p=0.002*

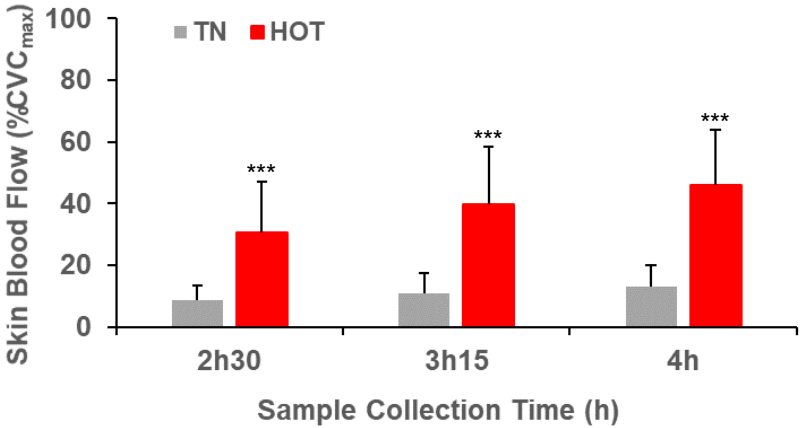


Figure 2. Skin blood flow over time (%CVCmax).

This represents preliminary data (unpublished)

LOCALIZED DERMAL ABSORPTION

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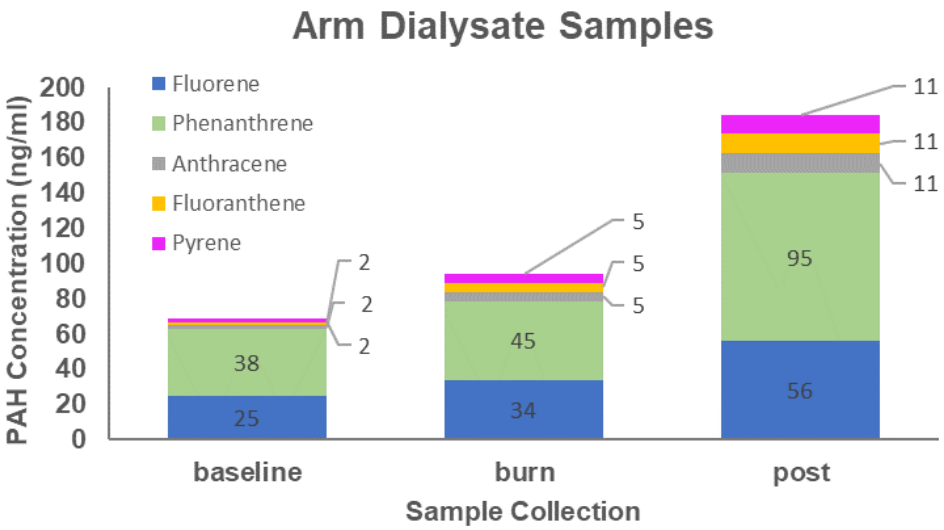


Figure 3. Concentration (ng/ml) of major polycyclic aromatic hydrocarbons in forearm dialysate of firefighters (n=7).

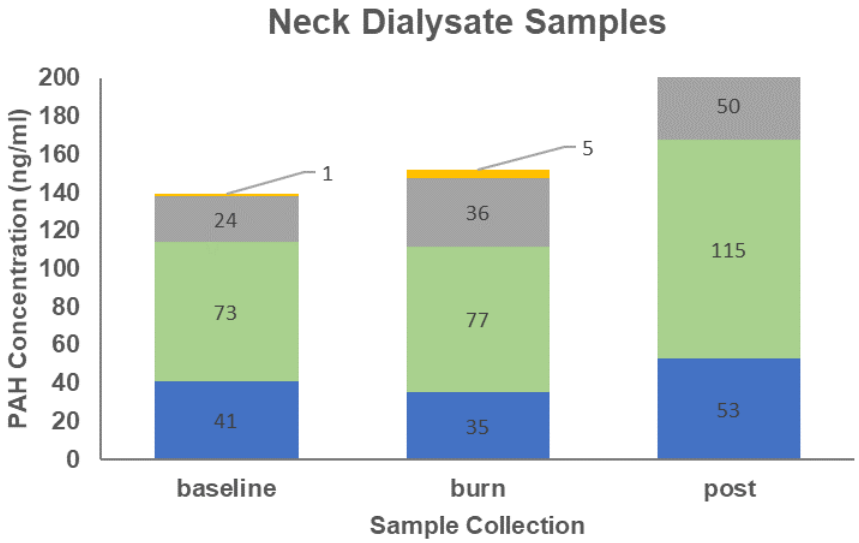
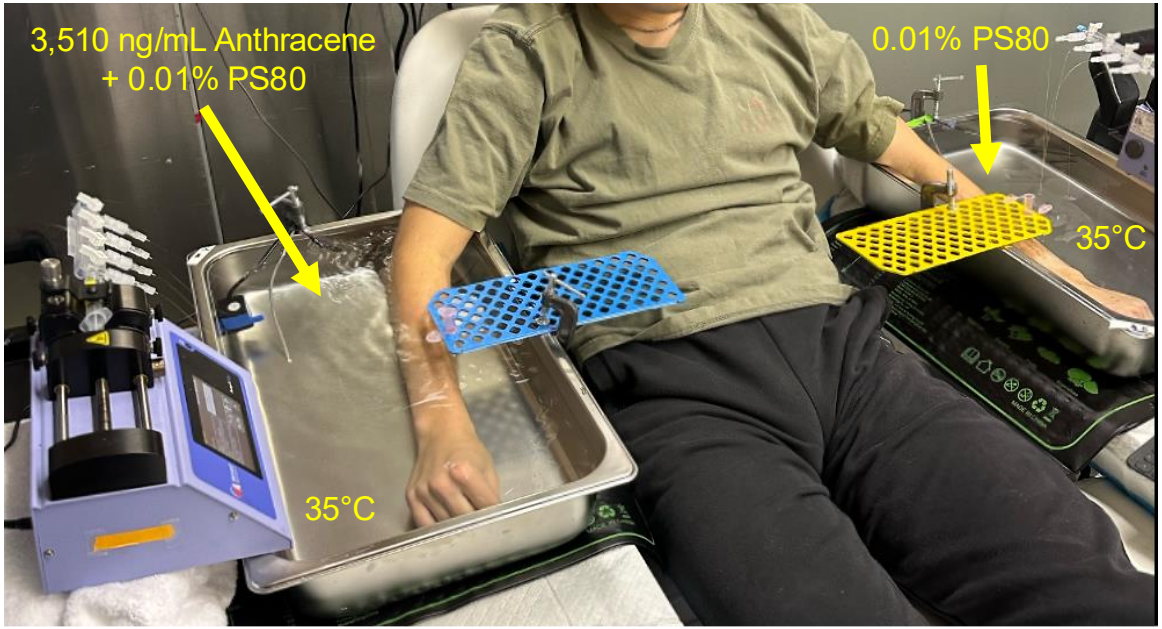


Figure 4. Concentration (ng/ml) of major polycyclic aromatic hydrocarbons in neck dialysate of firefighters (n=7).

This represents preliminary data (unpublished)

DERMAL ABSORPTION MODEL IN WATER

Developing a new localized model for dermal absorption of PAHs in water.



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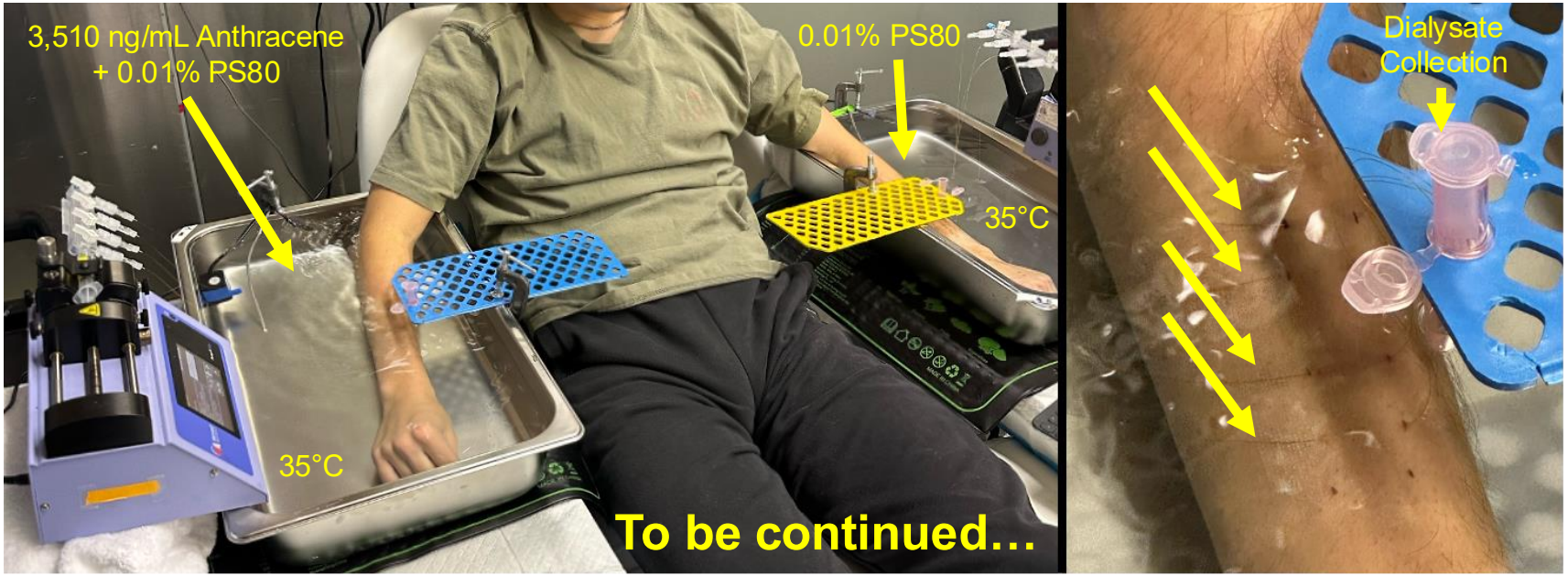

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Questions?

(N00014-23-1-2464)