



# Assessing *In Situ* Forming Implant Formulations Using *In Vivo* Imaging

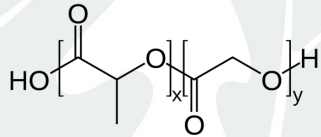
Xinhao Lin<sup>1</sup>, André O'Reilly Beringhs<sup>3</sup>, Derek Hargrove<sup>1</sup>,  
Michael Jay<sup>2</sup>, Yan Wang<sup>3</sup>, Qin Bin<sup>3</sup>, Xiuling Lu<sup>1</sup> \*

<sup>1</sup> Department of Pharmaceutical Sciences, University of Connecticut, Storrs, CT

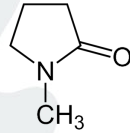
<sup>2</sup> Division of Pharmacoengineering and Molecular Pharmaceutics, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC

<sup>3</sup> Office of Research and Standards, Office of Generic Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD

# Assessing *In Situ* Forming Implant Formulations Using *In Vivo* Imaging

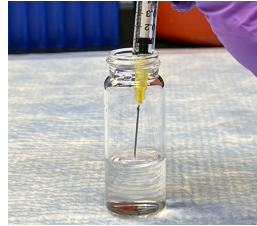


poly(lactic-co-glycolic acid)  
50:50, 25.8 kDa, Acid ending



NMP

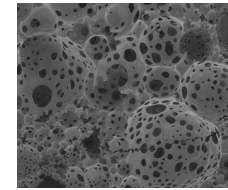
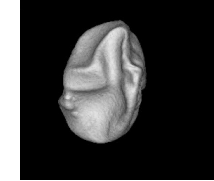
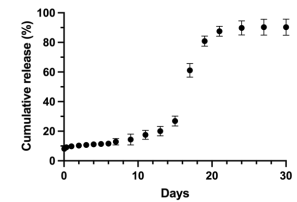
*in vitro*



*In vitro* release study

CT imaging

SEM



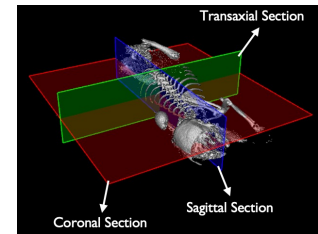
Eligard®  
Atrigel®

lohexol  
Leuprolide acetate  
(LA)

*in vivo*



CT imaging



## Objective:

Develop a non-invasive imaging approach to obtain improved understanding of both *in vitro* and *in vivo* implant formation and evaluate the impact of drugs on the morphology of the implant.

# Assessing *In Situ* Forming Implant Formulations Using *In Vivo* Imaging - CT imaging

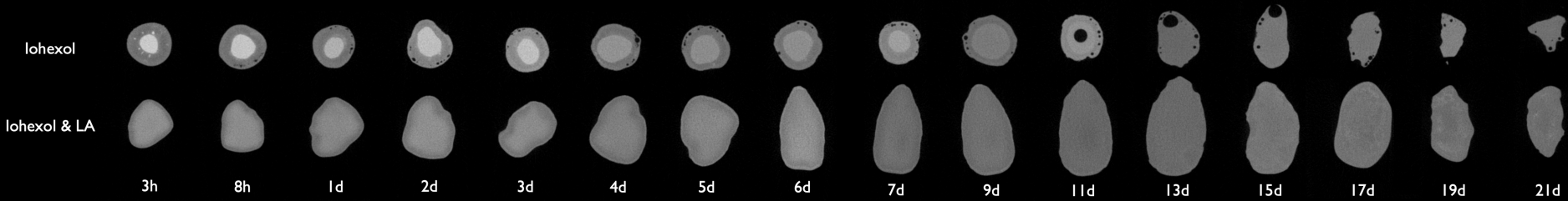


Figure 1. IVIS (*in vivo* imaging system) spectrum CT images showing the formation of *in vitro* formed implants with different drug compositions

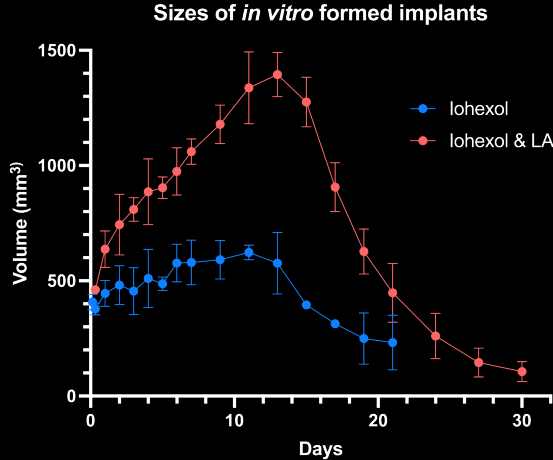


Figure 2. Mean and standard deviation of the volume of *in vitro* formed implants (n=3)

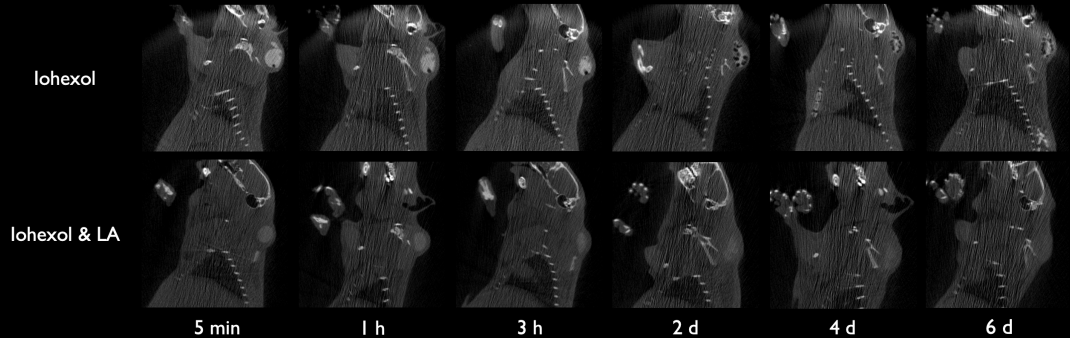


Figure 3. IVIS spectrum CT images showing the formation of *in vivo* formed implants with different drug compositions

# Assessing *In Situ* Forming Implant Formulations Using *In Vivo* Imaging

## - SEM & *In vitro* release study

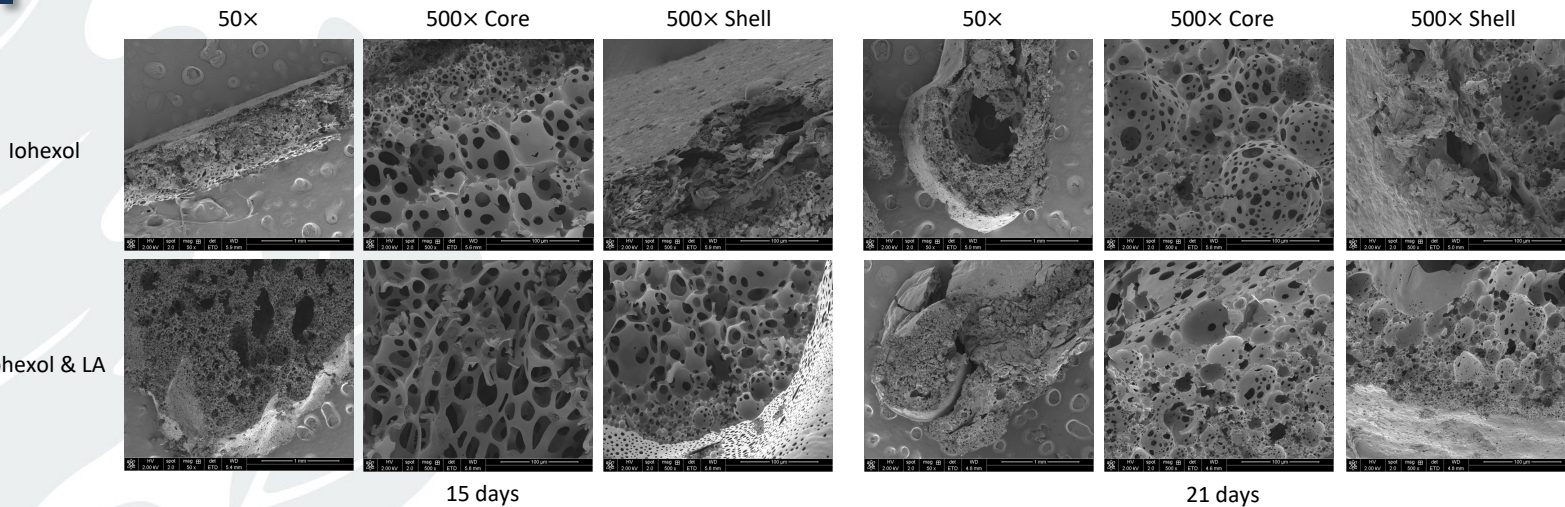


Figure 4. SEM images of *in vitro* formed implants.

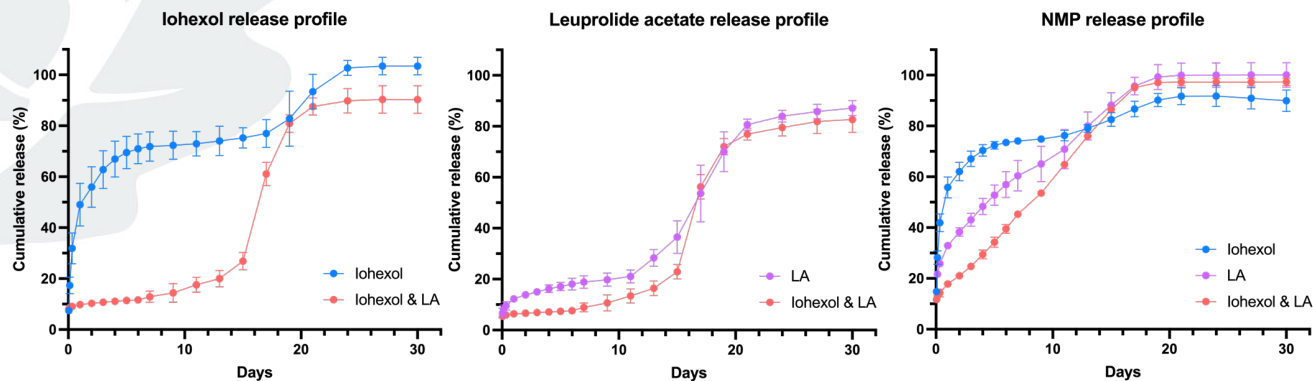


Figure 5. Mean and standard deviation of *in vitro* release profiles of *in vitro* formed implants (n=3; Iohexol: PLGA + Iohexol; LA: PLGA + LA; Iohexol & LA: PLGA + Iohexol + LA)

# Assessing *In Situ* Forming Implant Formulations Using *In Vivo* Imaging

## - Conclusion

- Addition of leuprolide acetate changes the inner structure of both *in vitro* and *in vivo* formed implants.
- Scattering of iohexol from the core and formation of small black cavities in the shell may be caused by the fast solvent exchange, which is supported by the *in vitro* release profile of NMP.
- Both iohexol and leuprolide acetate show a bi-phasic release profile and addition of leuprolide acetate inhibits the burst release of iohexol.
- *In vivo* imaging of implants provides a critical value for implant evaluation.

**Acknowledgement:** U.S. Food and Drug Administration's financial support (BAA contract :75F40120C00136).