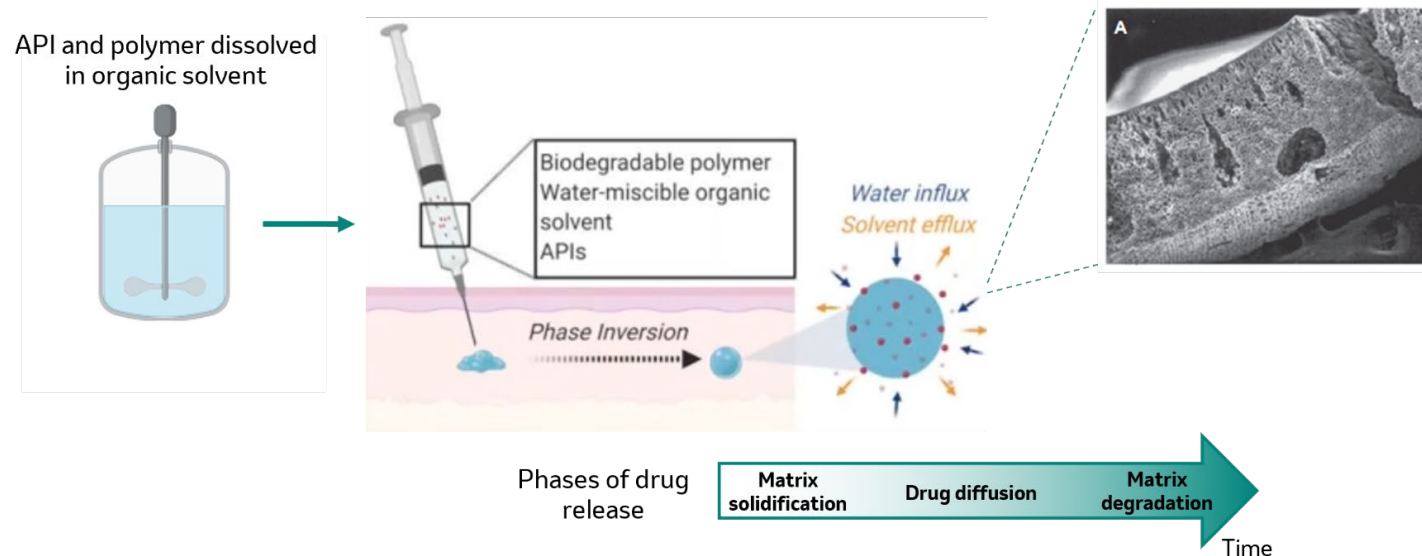


Evaluation of Long-Acting Injectable In-Situ Forming Gels using in vivo and in vitro MRI

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PLGA In-Situ Forming Gel (ISG) Mechanism



- API and polymer are dissolved in organic solvent.
- Both precipitate upon administration through solvent exchange with physiological fluid.
 - *In situ* depot forms
- Release rate controlled by API diffusion through polymer matrix and polymer degradation.

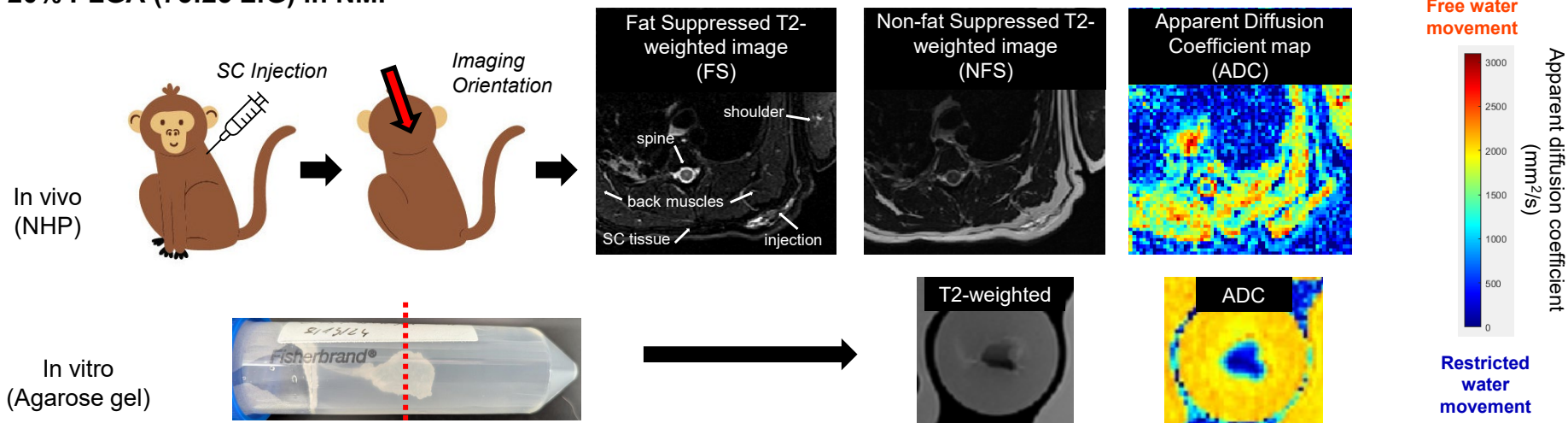
Parent et al., *Journal of Controlled Release* 2013, 172, 292-304. <https://doi.org/10.1016/j.jconrel.2013.08.024> ; Young I, Benhabbour SR et al. CROI, 2022 (LAPaL)

MR Imaging of ISG formulations

Study Questions

- Can we observe the different phases of this dynamic formulation using MRI?
- What is the physiological response to in-situ forming gels?

20% PLGA (75:25 L:G) in NMP

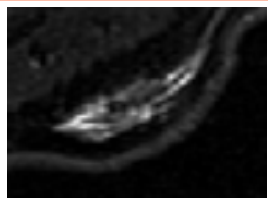


Can we observe the different phases of the ISG using MRI?

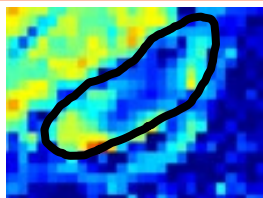
Phase Inversion

1 hour

T2-weighted Anatomical

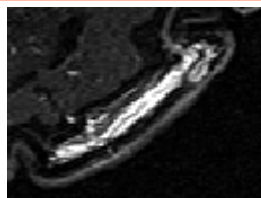


Apparent Diffusion Coefficient

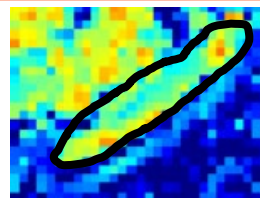


3 days

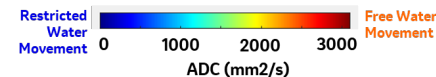
T2-weighted Anatomical



Apparent Diffusion Coefficient

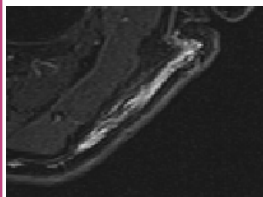


Phase inversion dynamics are evident in water diffusion images, showing a lack of water at the site immediately after injection (when solvent is present) and an increase in water content days later.



Polymer Degradation

Week 1



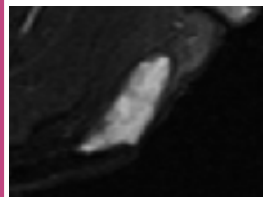
Week 4



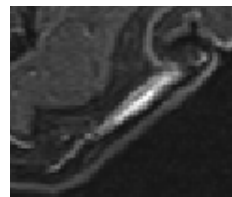
Week 12



Week 25



Week 35

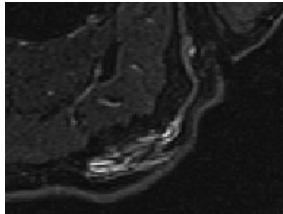
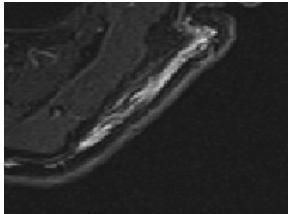
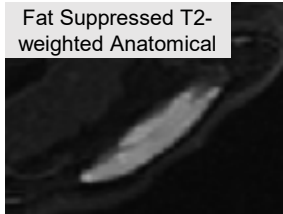
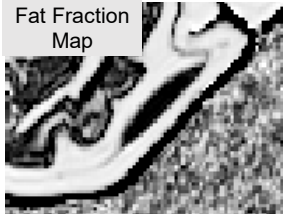


Polymer degradation is illustrated by a reduction in depot size over time.

Michal Tomaszewski

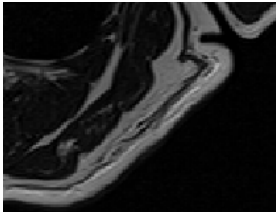
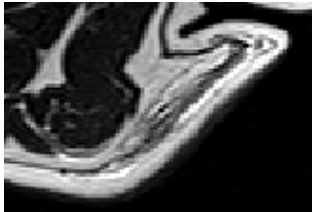
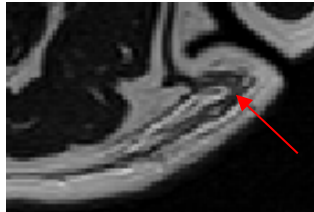
What is the physiological response to in-situ forming gels?

SC Tissue

Hour 1	Week 1	Week 18	
		 Fat Suppressed T2-weighted Anatomical	 Fat Fraction Map

During early time points, the depot forms heterogeneously throughout the subcutaneous (SC) tissue, eventually reaching equilibrium and excluding SC fat at later stages

Granuloma Formation

	Week 1	Week 2	Week 3
Non-Fat Suppressed T2-weighted Anatomical Images			

Granuloma formation is evident in non-fat suppressed T2-weighted images by week 3

Michal Tomaszewski

MR Imaging of in-situ forming gel formulations

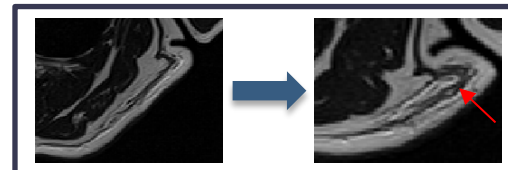
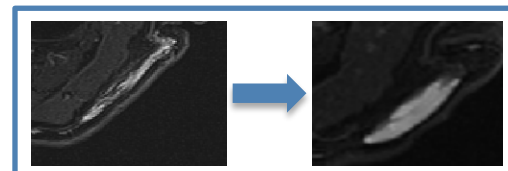
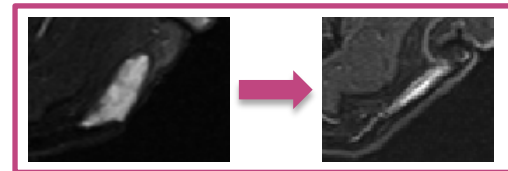
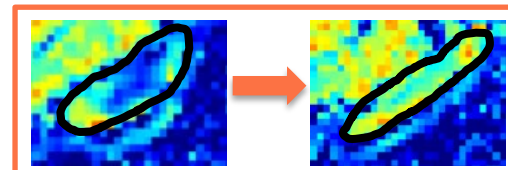
MRI was used to answer the following:

✓ Can we observe the different phases of this dynamic formulation using MRI?

- Phase Inversion – Water diffusion measurement imaging
- Polymer Degradation – Depot size measurements

✓ What is the physiological response to these types of injections?

- Evolution of formulation within SC tissue – Anatomical imaging
- Granuloma Formation – Non-fat suppressed imaging



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