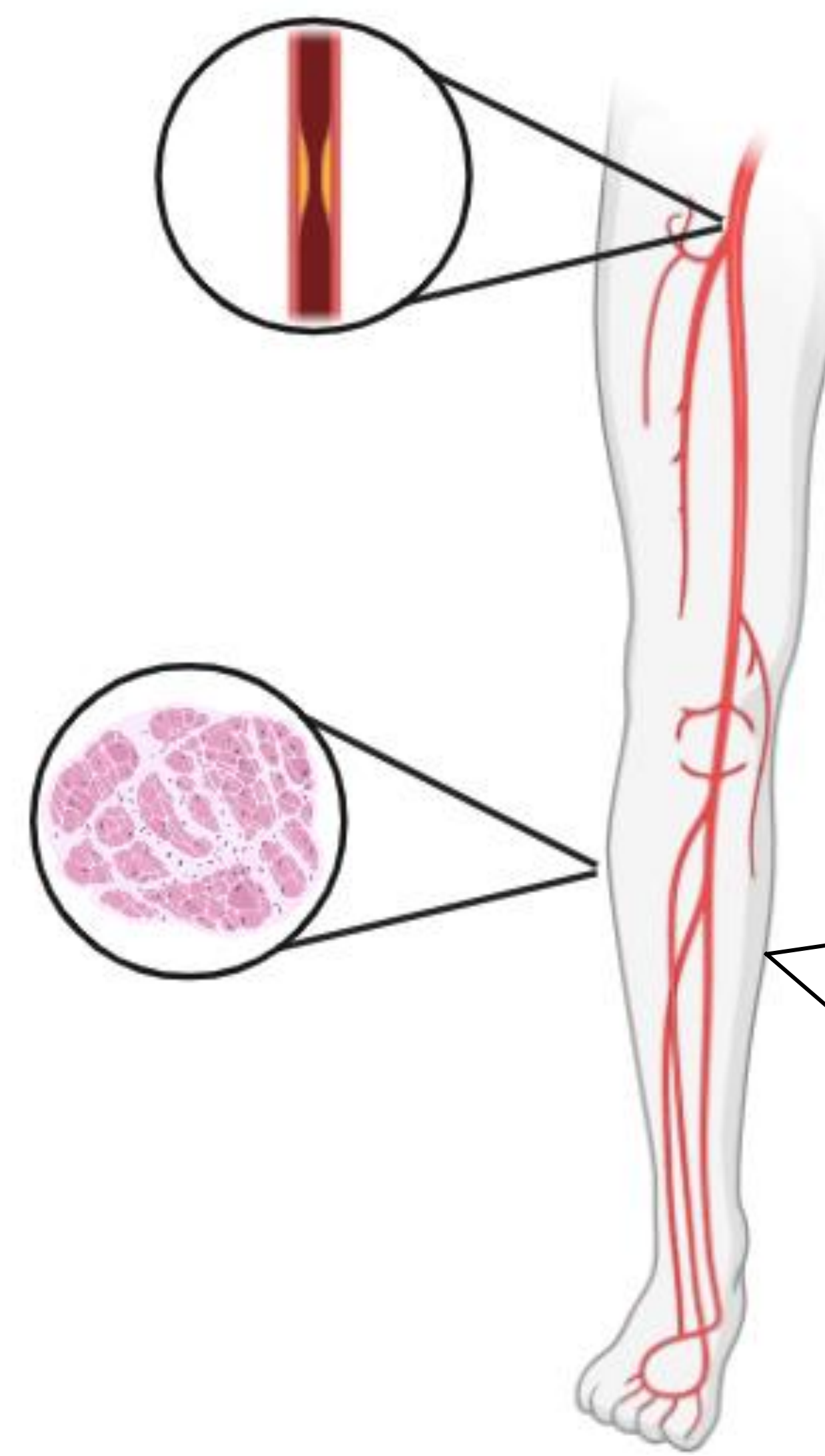
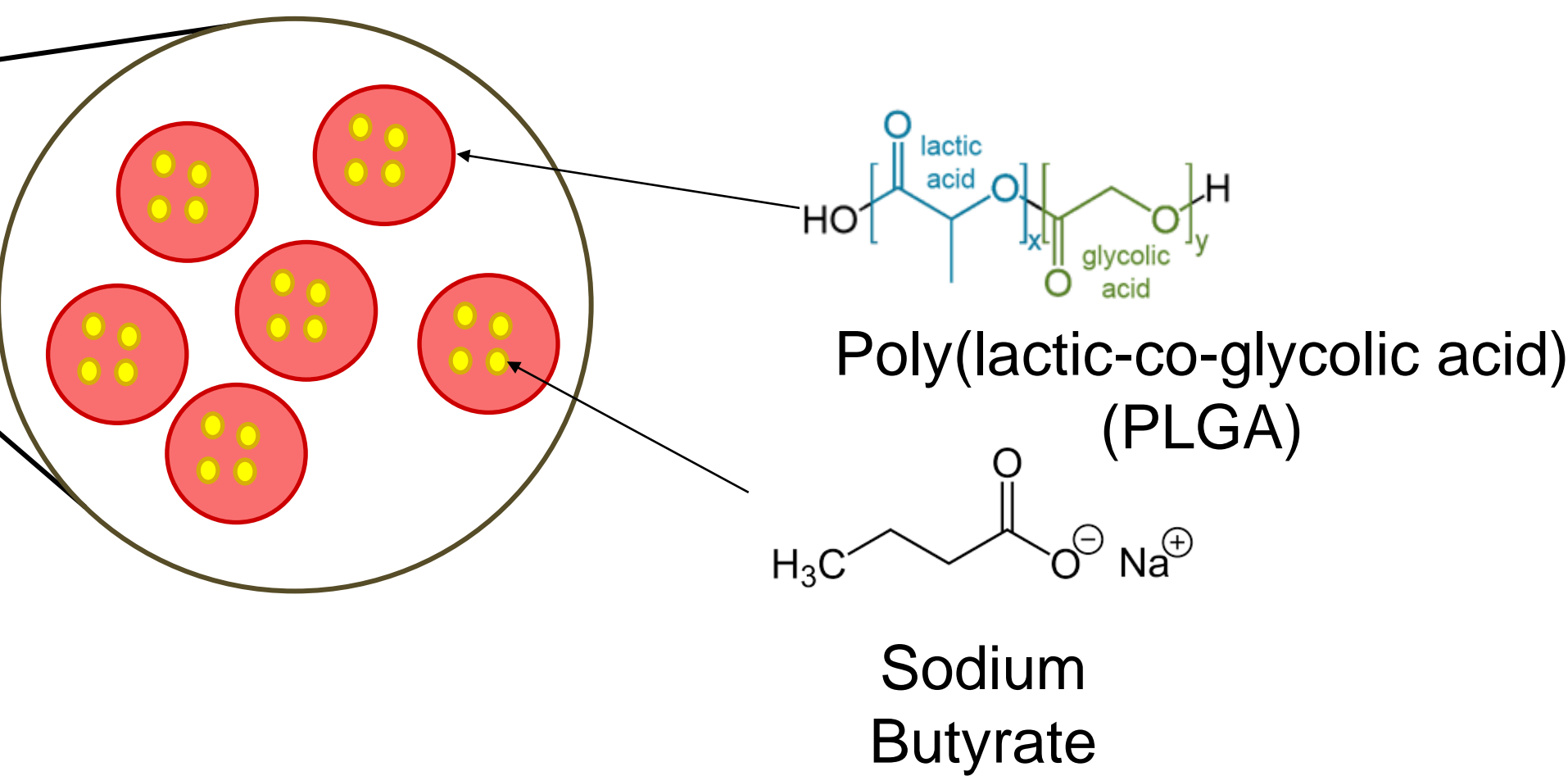


Introduction

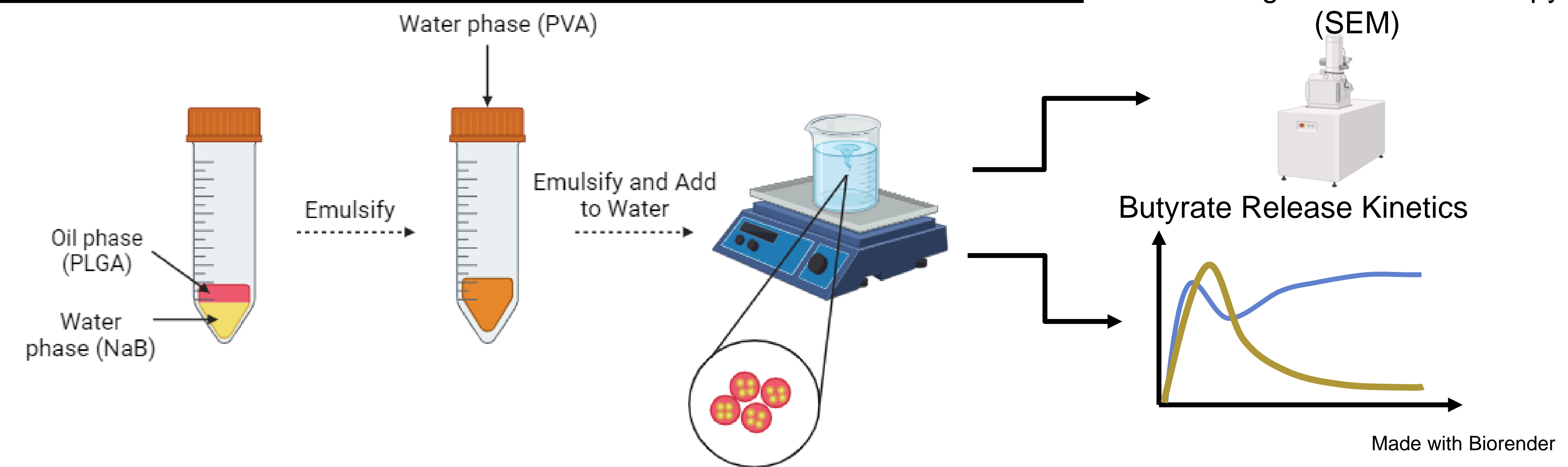


- **Critical limb threatening ischemia:** blockages in the lower extremity vasculature prevent sufficient blood flow → local oxygen and nutrient deficiency, **muscle degeneration**, fat infiltration¹
- **Sodium butyrate:** short chain fatty acid, seen to ameliorate fibrosis and restore contractility to ischemic cardiac tissue²
- **Hypothesis:** Sustained butyrate delivered locally via PLGA microspheres to ischemic tissue will prevent muscle degeneration and improve tissue regeneration and recovery from ischemic injury.

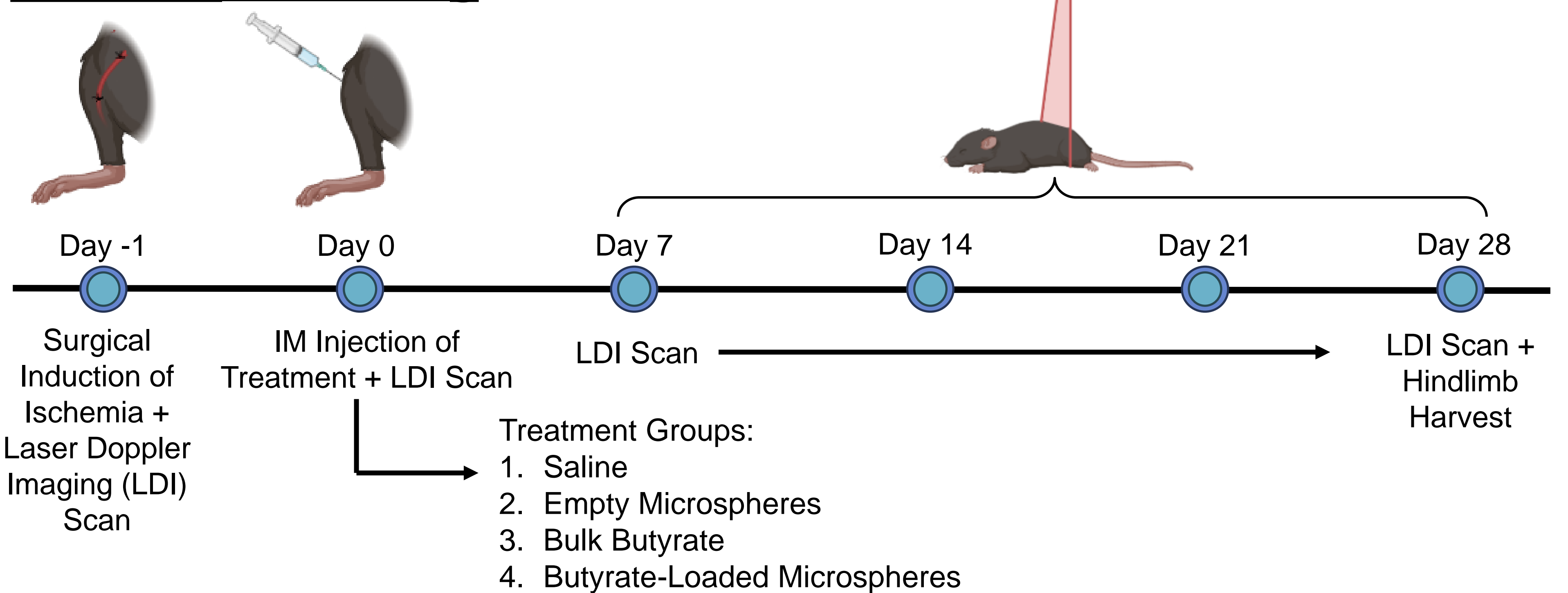


Methods

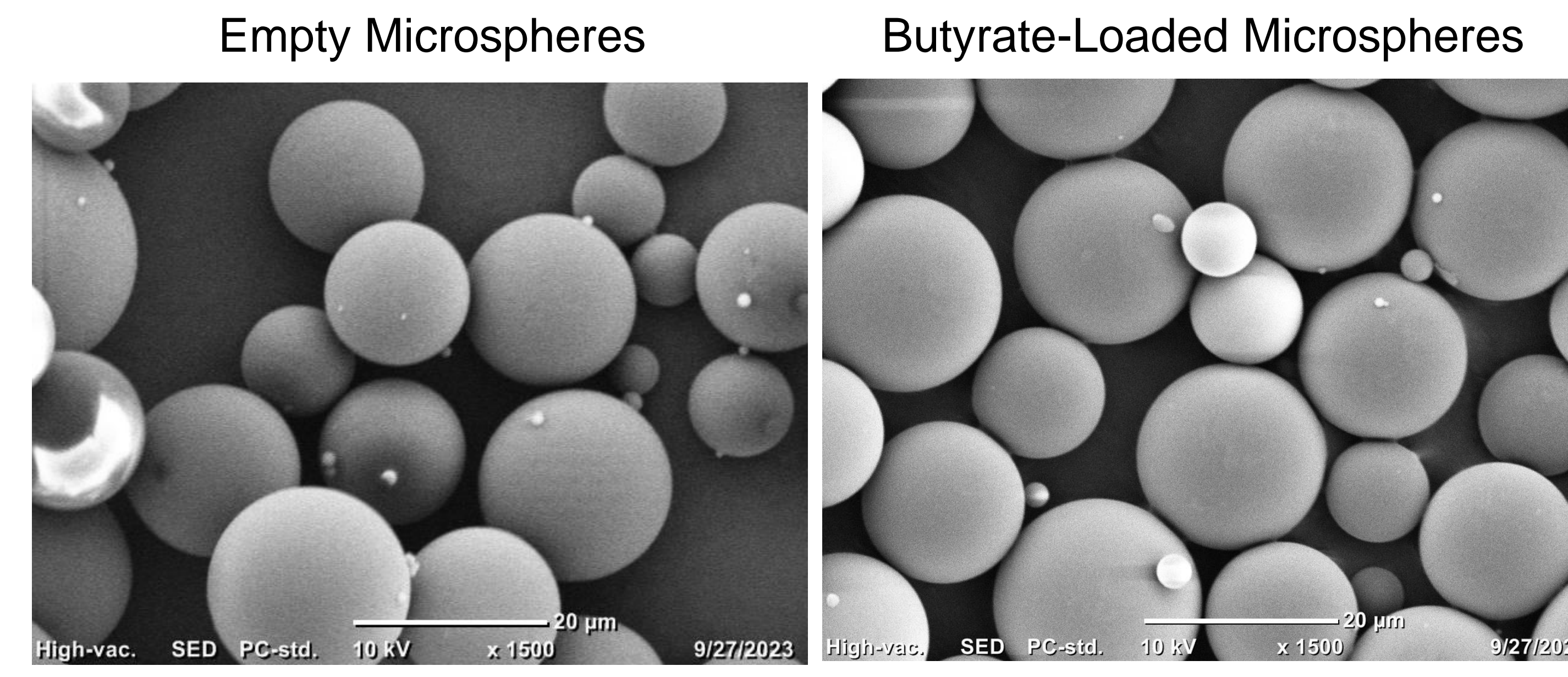
Microsphere Fabrication and Characterization



Pilot *in vivo* Testing



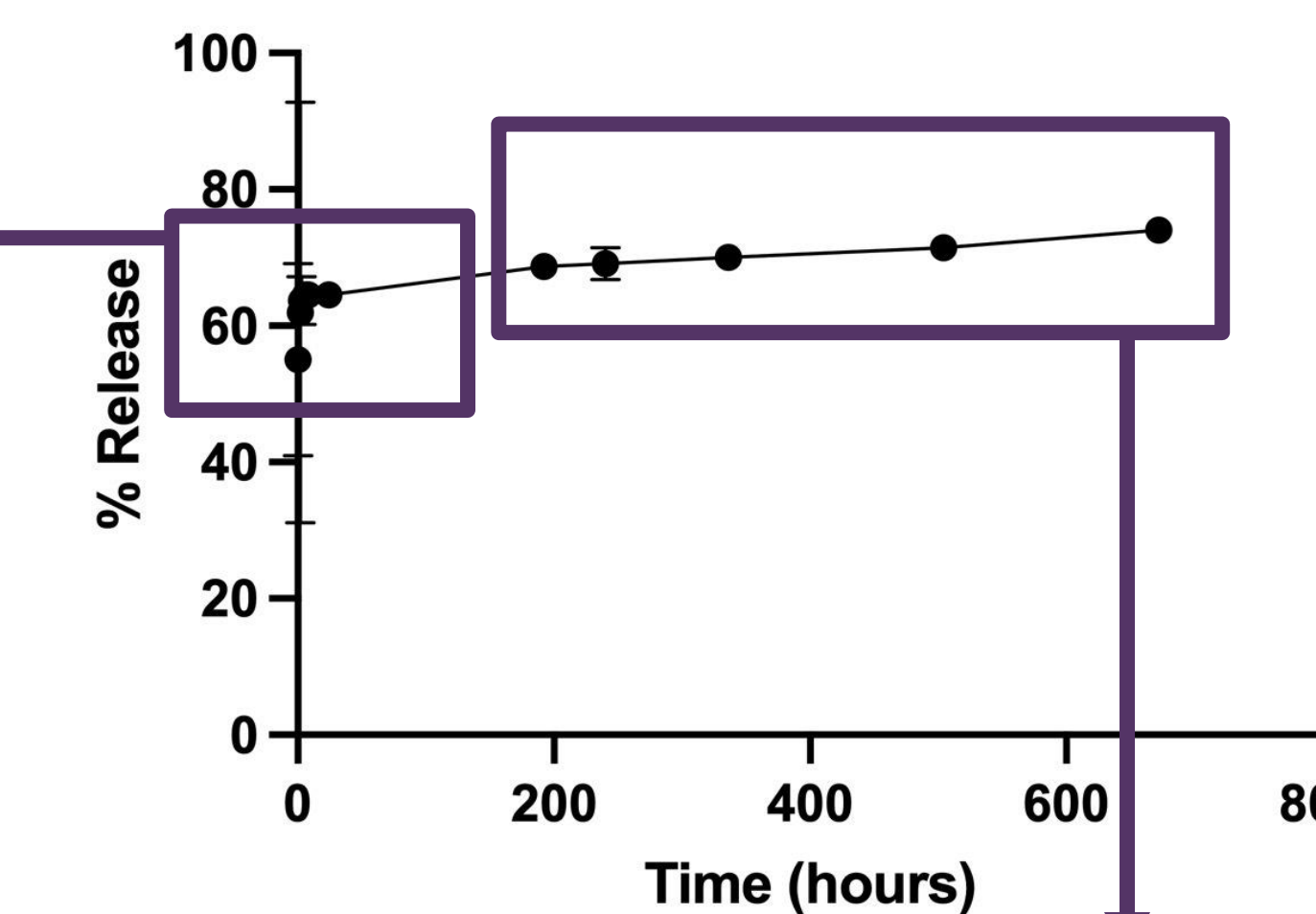
SEM Incorporation of butyrate did not affect surface topography or self assembly of microspheres



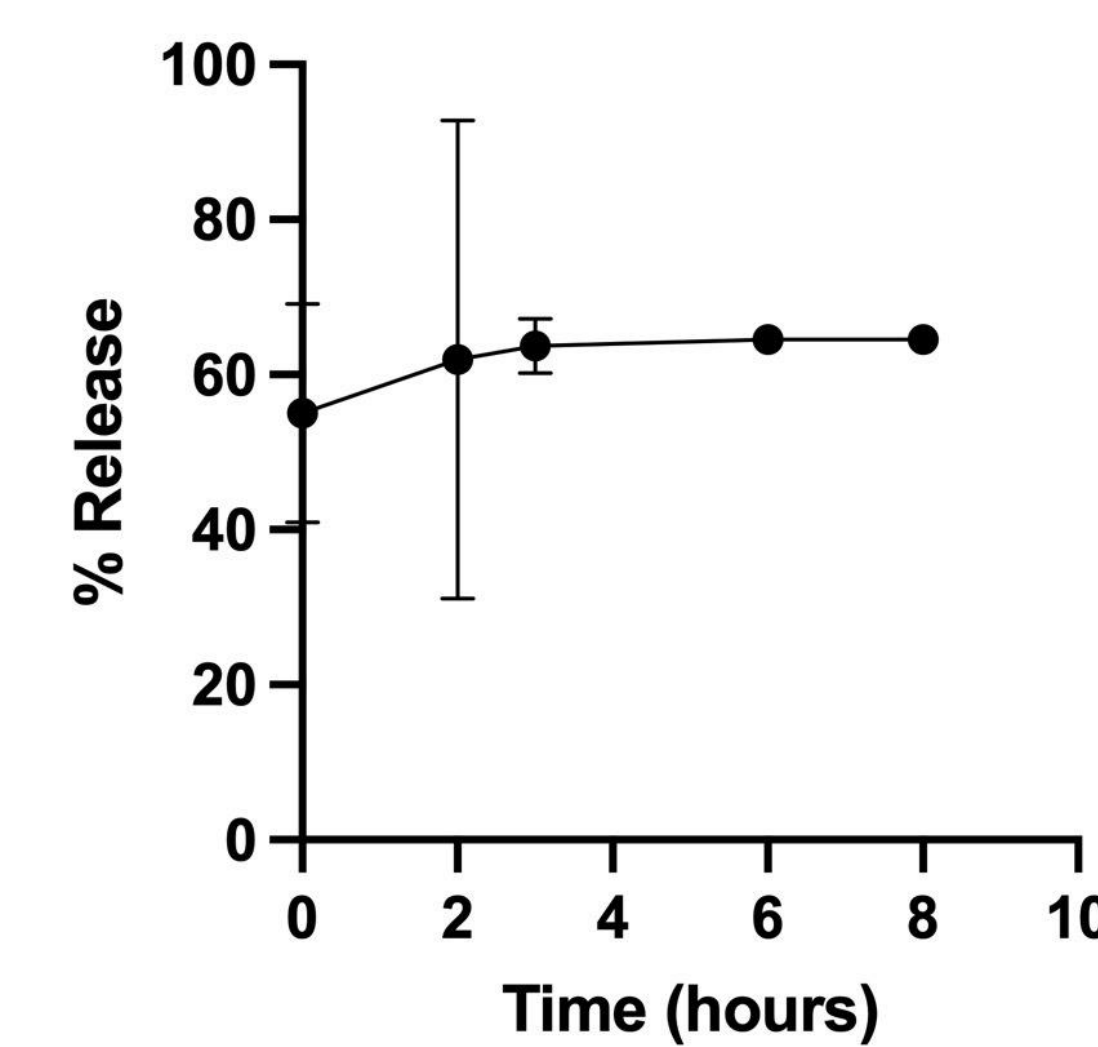
Microsphere Physical Characteristics		
	Empty Microspheres	Butyrate-Loaded Microspheres
Average Diameter (µm)	79.27±56.752	50.69±42.659
Loading Efficiency (%)	N/A	54.3±0.56

Release kinetics show that 50% of butyrate is released within the first few hours, followed by a sustained release

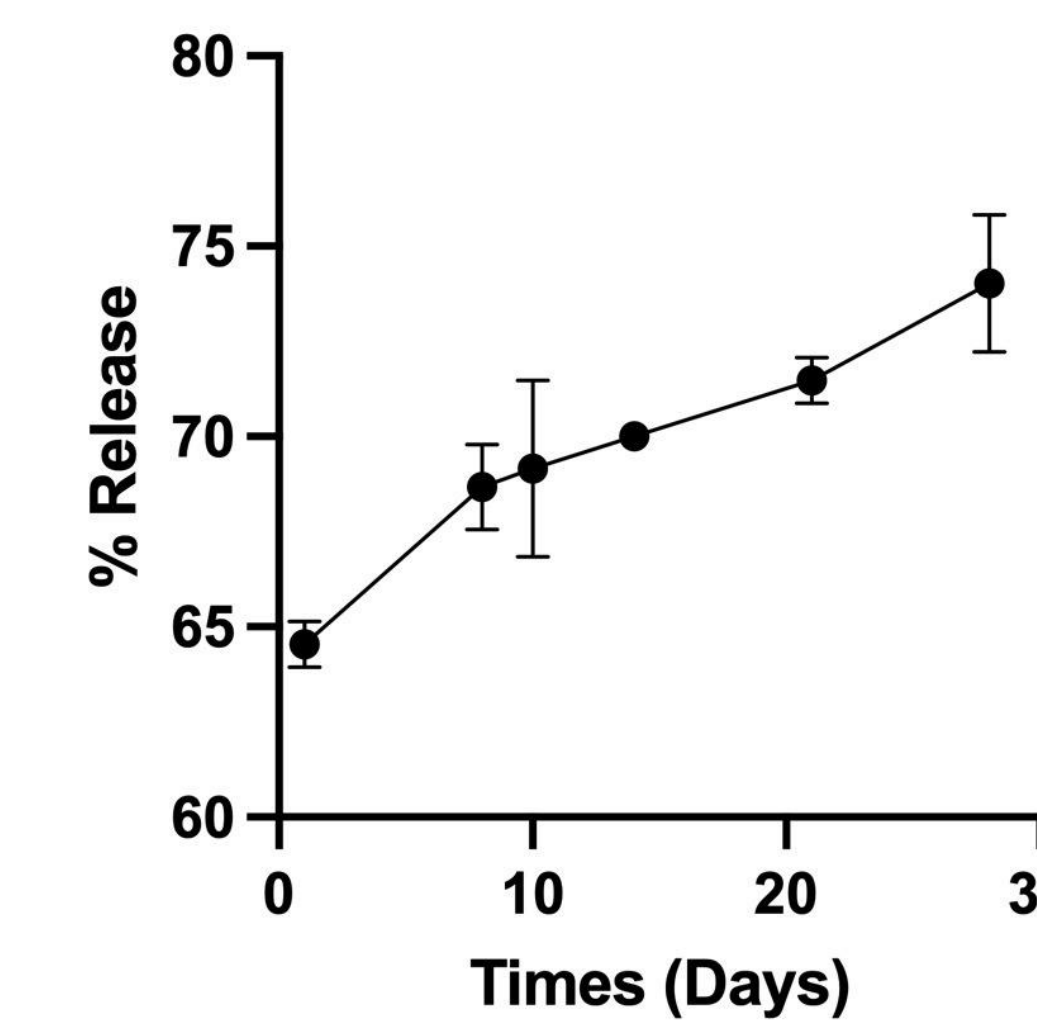
Sodium Butyrate Release Curve



Sodium Butyrate Release Curve (8 Hours)

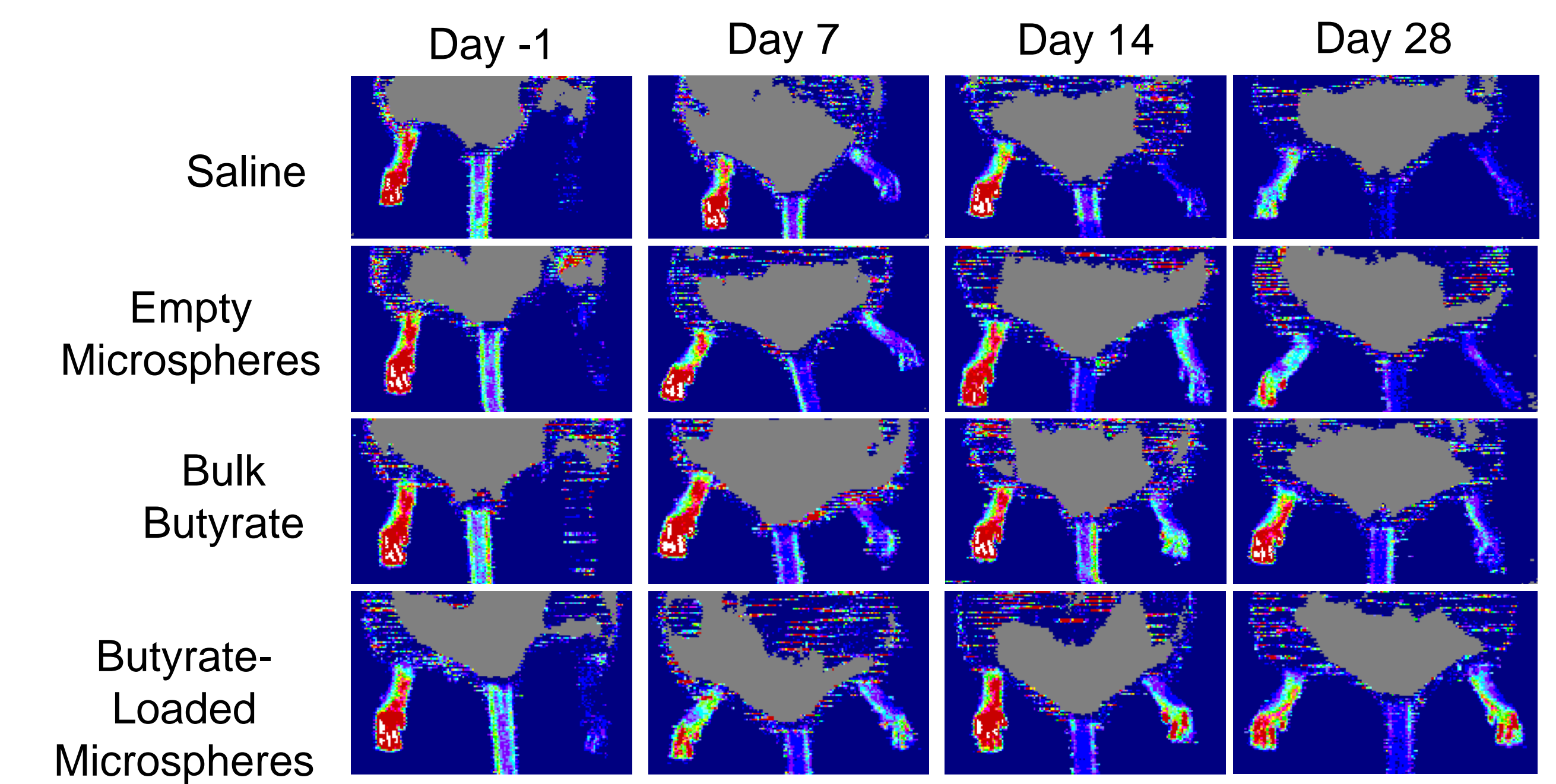


Sodium Butyrate Release Curve (1 month)

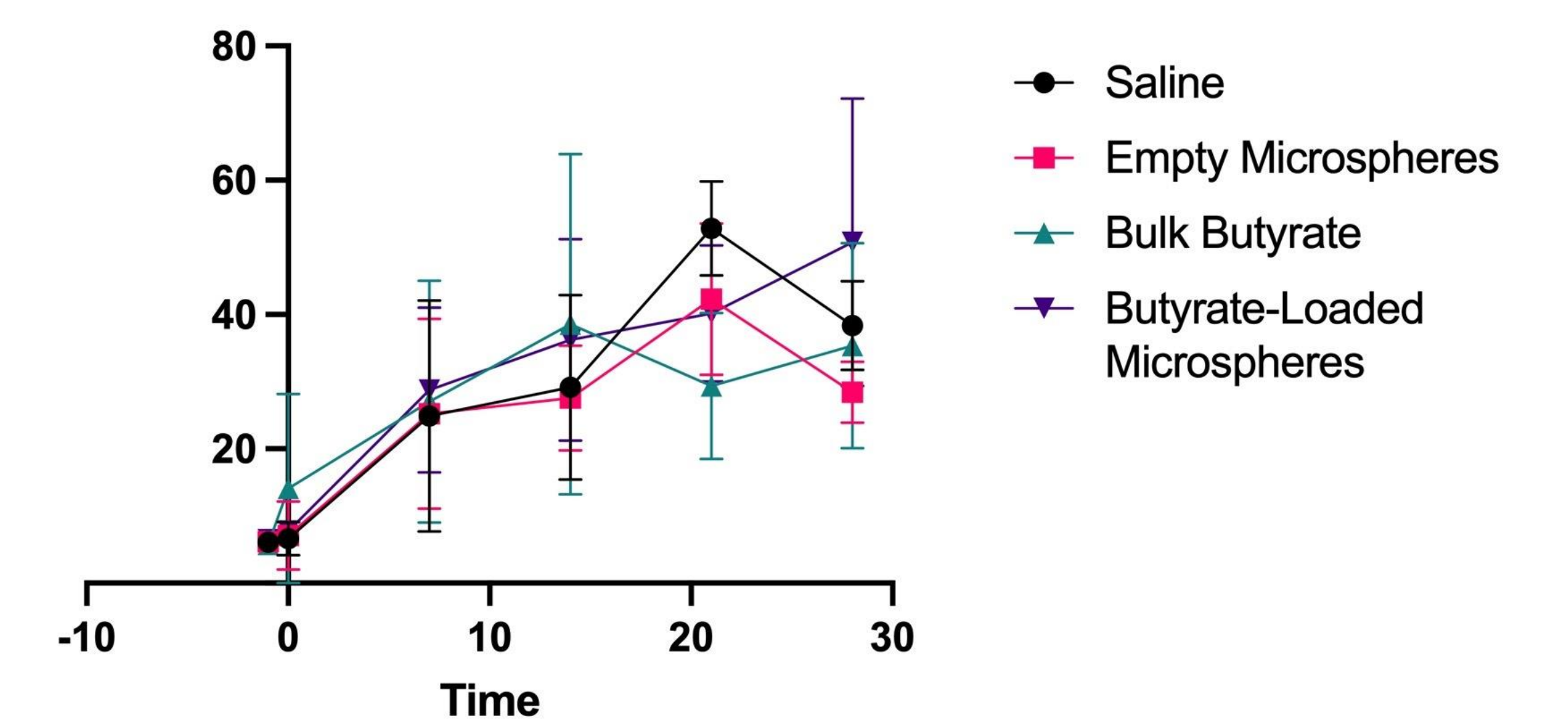


Results

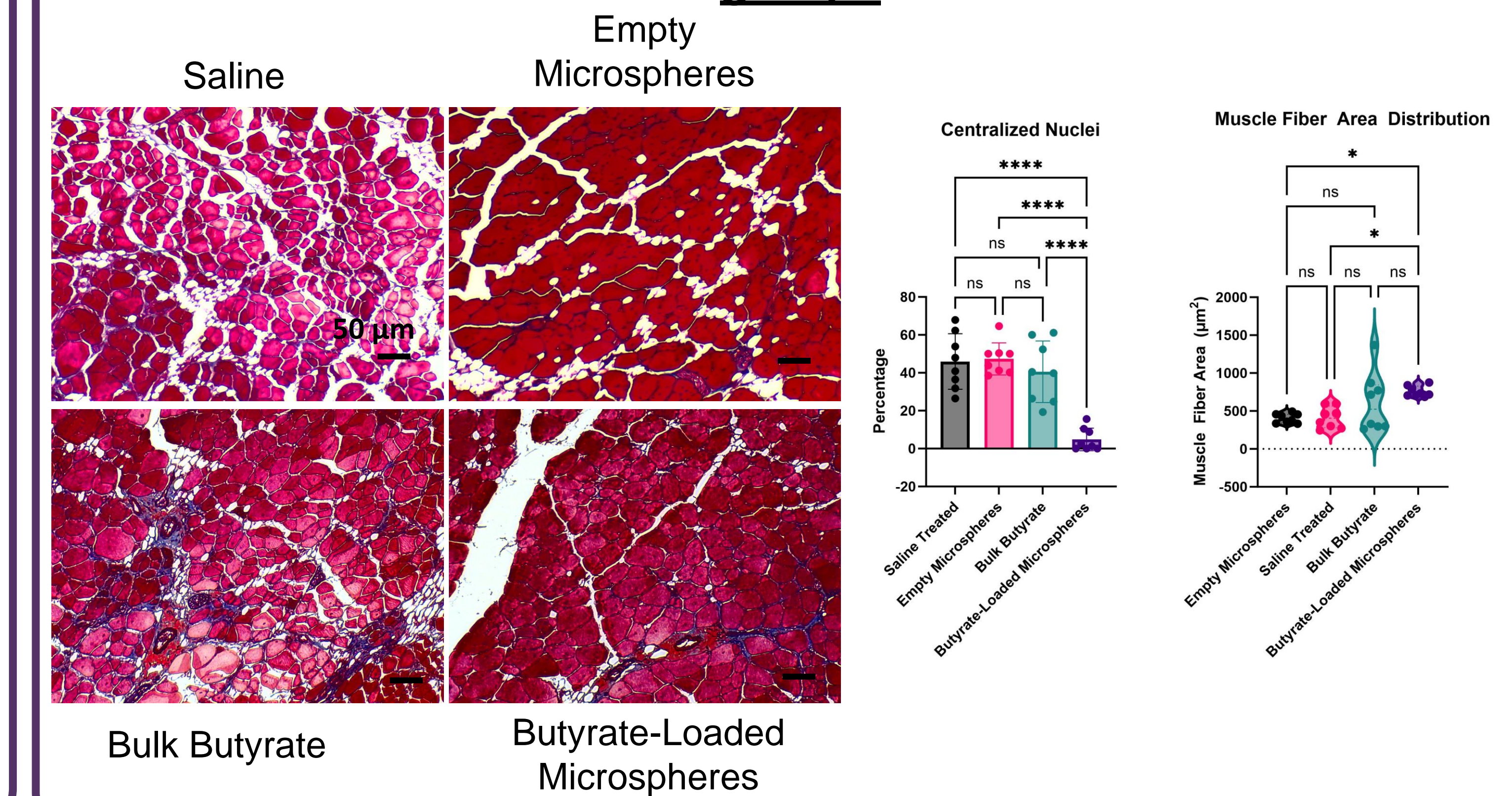
Butyrate treatment did not significantly impact perfusion over one month



Ischemic Limb Reperfusion



Muscle fibers have higher regularity in size in butyrate treated groups



Future Directions

- Quantitative analysis of percentage of fibrotic tissue and fatty infiltration will be conducted
- If no significant difference in muscle fiber diameter/regeneration is observed, *in vitro* dosage studies will be conducted to determine ideal dosage for skeletal muscle
- Dosage studies conducted under hypoxic conditions → myoblast behavior (proliferation, differentiation) also will be quantified *in vitro* to determine butyrate's effect on muscle cells under hypoxic conditions

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References

1. Weiss, D. J. *et al.* Oxidative damage and myofiber degeneration in the gastrocnemius of patients with peripheral arterial disease. *J. Transl. Med.* 11, 230 (2013).
2. Cheng, P. *et al.* PLGA-PNIPAM Microspheres Loaded with the Gastrointestinal Nutrient NaB Ameliorate Cardiac Dysfunction by Activating Sirt3 in Acute Myocardial Infarction. *Adv. Sci.* 3, 1600254 (2016).