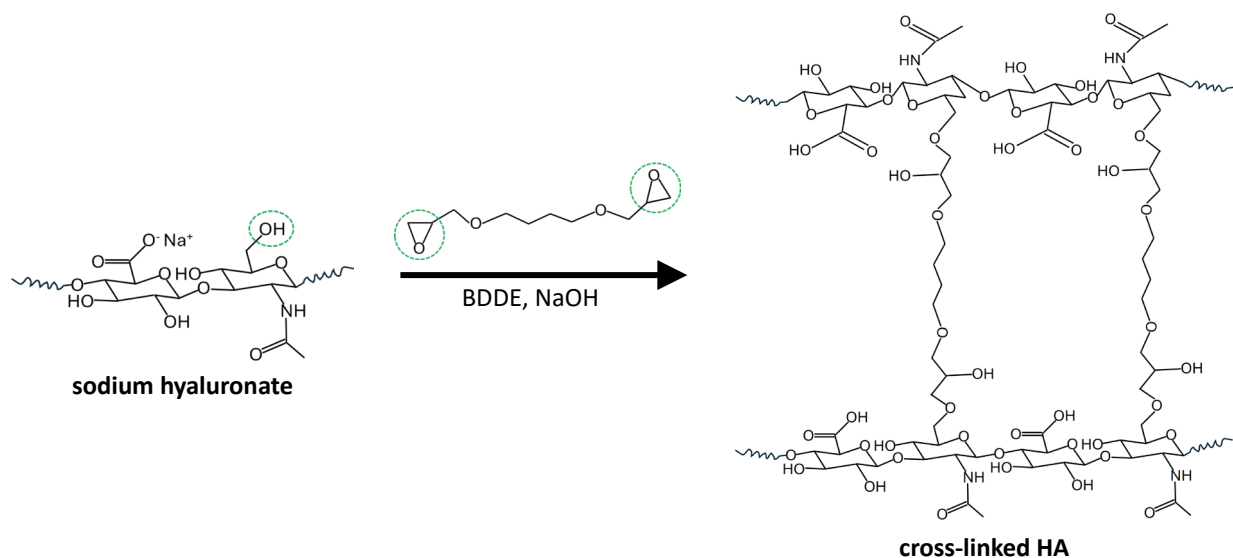
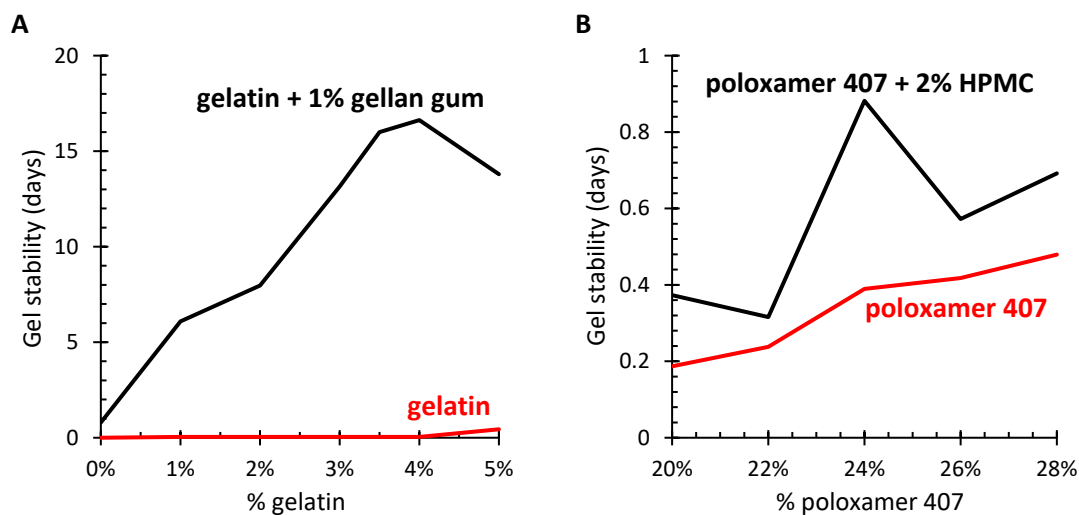


Supplemental materials

Patel AK, et al. (2026) "Radiopaque microsphere-hydrogel composite for extended-release intratumoral immunotherapy in a large animal model." *Drug Delivery and Translational Research*.



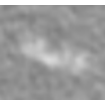
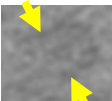
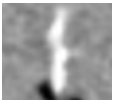
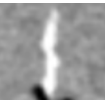
Supplemental Figure 1. Cross linking hyaluronic acid using BDDE (1,4-butanediol diglycidyl ether).



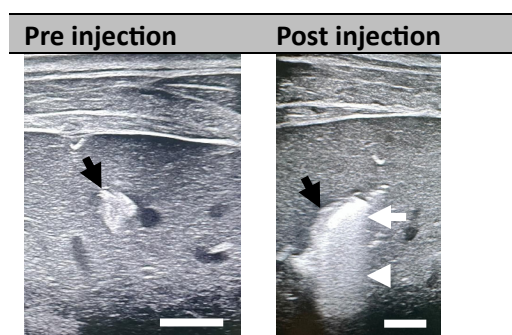
Supplemental Figure 2. Gel stability *in vitro*. A. Gellan gum improves the stability of gelatin gels. B. HPMC improves the stability of poloxamer 407 gels.

Gel	Gel stability (days)
22% poloxamer 407	0.24
22% poloxamer 407 + 2% HPMC	0.32
3.5% gelatin	0.04
3.5% gelatin + 1% gellan gum	16
4% hyaluronic acid	14
4% cross-linked hyaluronic acid	19
5% hyaluronic acid	28
5% cross-linked hyaluronic acid	>30

Supplemental Table 1. Gel stability *in vitro*.

Drug / Drug carrier	1 minute	1 hour	2 days	Burst release	Half-life	Off target
Iohexol / Water				63%	3.9 min	*
Iohexol / Cross-linked hyaluronic acid				9%	5.3 hr	
Erythrosine / Microspheres				93%	37 hr	*
Erythrosine / Microspheres in cross-linked hyaluronic acid				12%	6.3 days	

Supplemental Figure 3. The microsphere gel has low burst release, and the longest half-life, for local drug delivery into pig liver. Serial CT shows biodistribution and drug release kinetics, after injection of 1 ml of various drugs and drug carriers into pig liver. Erythrosine is a negatively charged iodinated compound, which enables evaluation of biodistribution and drug release kinetics on CT. 2 days after injection, the cross-linked hyaluronic acid is retained at the injection site (arrows), while iohexol washes out. On the other hand, erythrosine is retained in the microsphere gel, due to electrostatic loading onto the microspheres. Injection of microspheres alone into pig liver results in high burst release and off-target delivery. * = injected material seen in portal vein, hepatic vein, bile ducts, or peritoneum.



Supplemental Figure 4. Ultrasound-guided injection of CpG-STAT3ASO microsphere gel (white arrow) into a liver tumor (black arrow). Ring down artifact (white arrowhead) is seen. Scale bar is 1 cm.