Introduction
Recent publications have identified that local anesthetics uncouple insulin signaling by inhibiting p70s6k and lipid emulsion activates AMP-kinase (TSC2) following ischemia-reperfusion. Further, while it is clear that lipid emulsion exerts a cardioprotective effect, it is unclear through what pathway this effect functions. We hypothesized that bupivacaine uncouples insulin signaling with sensitization to insulin signaling during recovery and lipid emulsion activates insulin signaling, potentiating the recovery effect.

Methods
Sprague-Dawley rats received 10mg/kg Bupivacaine over 20s, followed by nothing or 10mL/kg 30% Intralipid. Following sacrifice at 0, 1, 5 and 10 minutes, hearts were frozen. An additional set of animals was given 10mg/kg Intralipid and sacrificed at 5 minutes or pre-treated with p70s6k inhibitor Wortmannin or LY294002 (in isolated hearts) then subjected to Bupivacaine. Protein was extracted and phosphorylation levels for protein in Figure 1 were assayed. Theoretical cardiac bupivacaine concentration based on radiolabel studies.

Results
Figure 1: Cardiac glycogen concentration for control hearts (n=9) and bupivacaine treated hearts in recovery (n=5) \( *: p=0.01 \).

Figure 2: Cardiac glycogen concentration for control (n=9) and bupivacaine treated hearts in recovery (n=5) **: \( p<0.05 \).

Future Implications
Bupivacaine toxicity titrates insulinergic signaling and the sensitization to Insulin-signaling use IRS1 dephosphorylation is required for recovery. Lipid emulsion potentiates the recovery by the ability to drive insulinergic signaling in the absence of toxicity. In addition to its ability to sequesrante ions, the benefit of lipid emulsion in combating cardiac toxicity may be modulated by its pro-insulinergic effect. This may have implications for treatment of xenobiotic drug overdose such as Calcium channel blockers or tricyclic antidepressants which are known to cause derangements in glucose homeostasis.

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Conclusion
Theoretical cardiac bupivacaine concentration based on radiolabel studies.