

## Decreased Reticuloendothelial System Clearance and Increased Blood Half-Life and Immune Cell Labeling for Nano- and Micron-Sized MRI Contrast Agents upon Pre-Treatment with Intralipid

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### Target Audience

Scientists who are interested in reducing the reticuloendothelial system (RES) clearance of magnetic resonance imaging (MRI) contrast agents and imaging more diverse targets other than the liver.

### Purpose

Non-invasive *in-vivo* MRI of monocytes/macrophages labeled with MRI contrast agents may lead to a better understanding of the pathogenesis of many diseases, including graft rejection, atherosclerotic plaques, tumors, abdominal aortic aneurysm, renal ischemia, Alzheimer's disease, etc. MRI contrast agents are taken up by the RES, in particular by liver Kupffer cells, which often contribute to the major loss of the agents in circulation<sup>1-4</sup>. Strategies that reduce liver uptake and prolong the circulation residence time of these MRI contrast agents can improve the *in-vivo* labeling efficiency of monocytes/macrophages and lower the required effective dose. In this study, we set out to find an FDA approved agent that could achieve this goal.

### Methods

In this study, two types of superparamagnetic iron-oxide based MRI contrast agents were applied to test our methodology: nano-sized ultra-small superparamagnetic iron-oxide (USPIO, with particle size ~30 nm in diameter) and micron-sized paramagnetic iron-oxide (MPIO, ~0.9 micron in diameter) particles. Intralipid 20.0%, approved by U.S. FDA in 1972 as a source of parenteral nutrition for patients and composed of 20% soybean oil, 1.2% egg-yolk phospholipids, and 2.25% glycerol, was intravenously administered at the clinical dose (2 g/kg) one hour before intravenous injection of MRI contrast agents.

### Results

Pre-treatment with Intralipid results a 45.1% reduction in liver uptake of USPIO particles, a 3.1-fold increase in blood half-life and a 2-fold increase in labeling efficiency of blood monocytes. Pre-treatment with Intralipid causes a 49.2% reduction in liver uptake of MPIO particles, a 2.5-fold increase in blood half-life and a 5-fold increase in monocyte labeling efficiency (**Figure 1**). Intralipid pre-treatment increases iron concentrations in MPIO-labeled blood monocytes from 0.82 pg Fe/monocyte to 2.60 pg Fe/monocyte.

### Discussion

Our findings can have broad applications for imaging and drug delivery, with the ability of nano- and micron-sized particles and carriers to target more diverse sites or organs, other than the liver.

### Conclusion

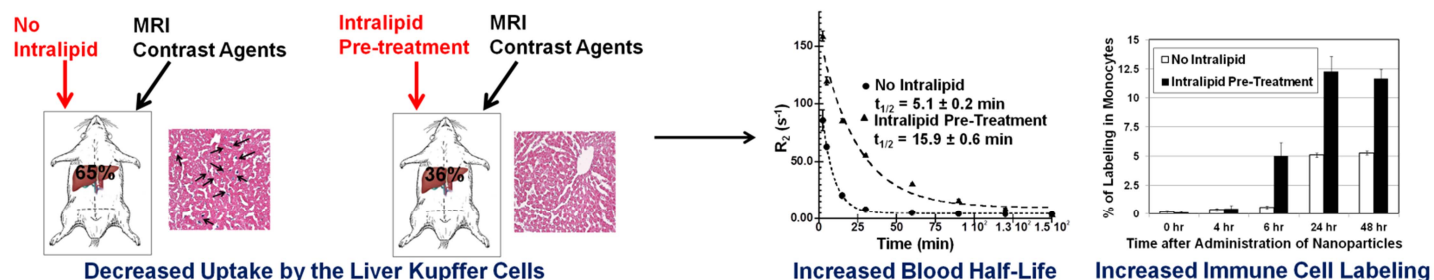
We have found that Intralipid significantly decreases initial RES uptake and increases *in-vivo* circulation and blood monocyte labeling efficiency of nano- and micron-sized superparamagnetic iron-oxide based MRI contrast agents.

### Acknowledgements

Our research is supported by National Institutes of Health (R01HL-081349 and P41EB-001977 to C. H.) and American Heart Association (10POST3010016 to L. L.).

### References

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**Figure 1.** Pre-treatment with Intralipid can result a ~50% decrease in liver uptake of nano- and micron-sized superparamagnetic iron-oxide based MRI contrast agents, resulting a ~3-fold increase in blood half-life and a 2- to 5-fold increase in the labeling efficiency of monocytes in the peripheral blood.