Contrast Enhancement Characteristics of a Lipid Nanoemulsion Contrast Agent for Micro-Computed Tomography

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OBJECTIVES

This study aimed to determine the contrast enhancement characteristics of a novel blood-pool nanoemulsion computed tomography (CT) contrast agent by determining the peak enhancement times for the blood in the heart, the liver, the lungs, and the spleen.

METHODS

The contrast agent analyzed is shown in Figure 1. The shell was made of 60% phospholipid 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) and of 40% lipid cholesterol. The core is made of 48 mg I/mL diluted Lipiodol (ethiodized oil; Guerbet LLC, Princeton, NJ). The dominant emulsion diameter was 267.2 nm with less prevalent groups of emulsions with diameters of 3.0 μm and 50.8 nm.

In vivo imaging was performed performed with 150 μL injections of the contrast agent administered via tail vein injections to 10-week-old C57Bl/6 female mice (N=6). Methods followed the work of Halajian et al.[1] with imaging timepoints of 0 min, 15 min, 30 min, 45 min, 1 h, 2 h, 4 h, 8 h, and 1 d post injection. An eXplore CT 120 (Trifoil Imaging, Chatsworth CA, USA) micro-CT scanner was used for imaging with a continuous rotation protocol (70 kV, 50 mA, 15 cGy). Images were reconstructed with an isotropic voxel spacing of 100 μm. After reconstruction, an edge-preserving bilateral filter was applied to the images in MATLAB (R2025b, The MathWorks, Inc.) in order to reduce image noise. Measurements were acquired with 1 mm^3 regions of interest in MicroView (version ABA2.2, TriFoil Imaging, Chatsworth CA, USA).

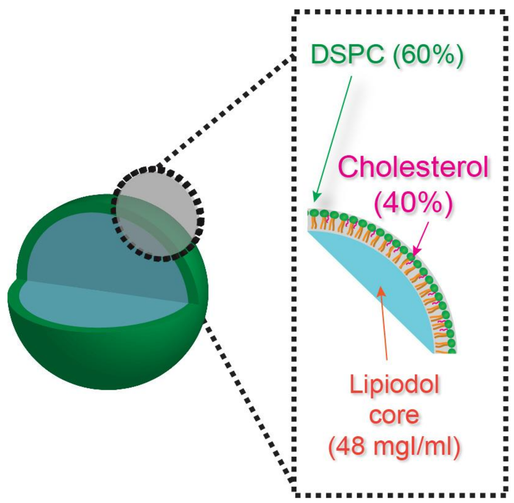

Figure 1. A schematic diagram of contrast agent. Its shell is composed of 60% phospholipid DSPC (green) and of 40% lipid cholesterol (magenta). The core consisted of Lipiodol (shown in blue).

Figure 2 shows parts of regions of interest used to measure Hounsfield Units (HU). The liver (Li), lateral to the gall bladder. The most posterior portion of the spleen (S). The right atrium of the heart (H). The right, anterior corner of the lung (Lu). Soft tissue (ST) muscle medial to the right fibula. Measurements for air (A) were recorded to ensure calibration of the micro-CT machine. Measurements were also made for the bladder (B) and kidneys (K), but with no definitive results found. Final reported values were the mean and standard deviation of data across all mice at each timepoint.

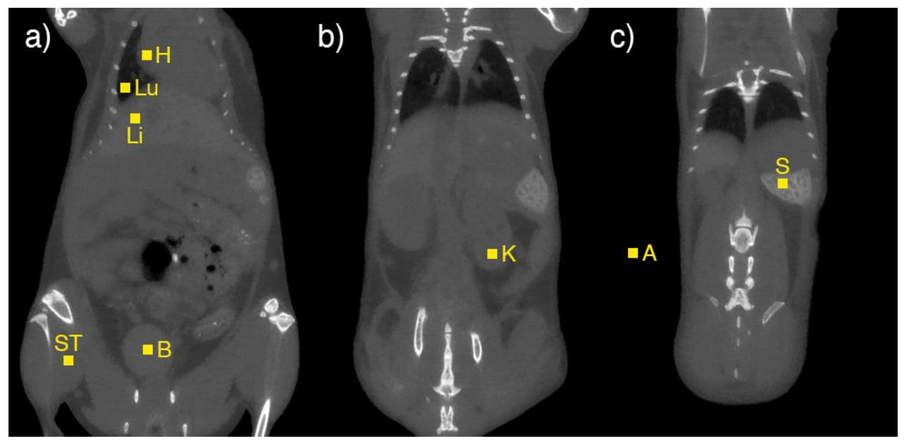

Figure 2. Micro-CT scan showing HU measurement locations. Locations shown for (a) the heart (H), lung (Lu), liver (Li), soft tissue (ST), and bladder (B). For (b) the kidney (K). For (c) the spleen (S) and air (A).

RESULTS

Figure 3 shows images during the time of peak enhancement for (a) the blood in the heart and (b) the liver for a single mouse. Poor enhancement (<100 HU) was found for both organs. Figure 4 shows the mean recorded HU values within organs for all mice vs the time post injection. Data is separated by whether the organ was a drug clearance pathway. The spleen had the greatest enhancement in HU. Based on previous work with a DSPC dominant shell with a Lipiodol core contrast agent[1], the liver had lower uptake than was expected.

The times to peak contrast enhancement were:

- Heart = 5.5 +/- 0.8 min
- Liver = 105.2 +/- 43.8 min
- Lungs = 50.3 +/- 18.8 min
- Spleen = 110.2 +/- 50.0 min

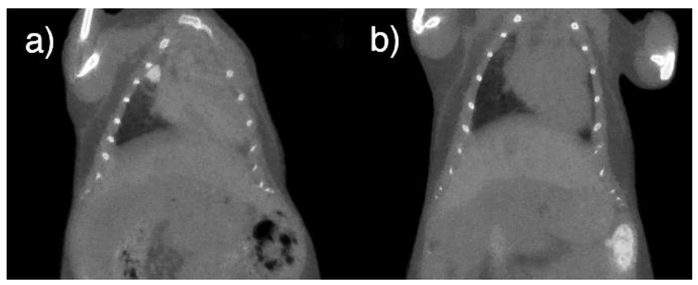

Figure 3. Micro-CT scans of a mouse. Scans are (a) immediately post injection for the time of peak blood enhancement and (b) 2 hr post injection for the time of peak liver enhancement.

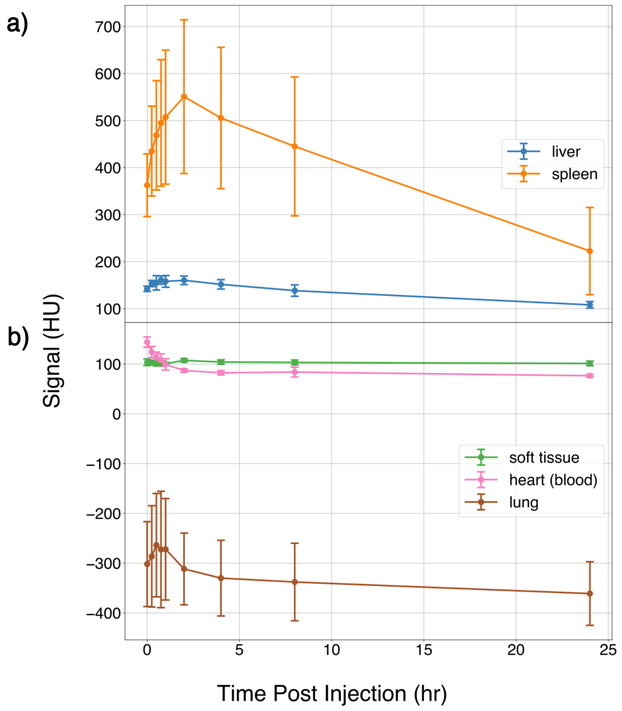

Figure 4. HU units recorded for (a) clearance pathway organs (liver and spleen) and (b) other organs (the heart, lung, and soft tissue). Data is plotted against the time post-injection in hours.

The large standard deviations of spleen and lung values may be due to combinations of differences in uptake of the contrast agent in, variability in the structure of, and/or variability in the composition of the lungs and spleens of mice.

An example of the differences in uptake between mice can be seen in Figure 5, where images are shown for 3 different mice close to the found peak enhancement time of the lungs. From (a) to (c), there is increasing signal intensity in the lungs of each mouse. Each organ was found to be more/less enhanced at the time of peak enhancement was similarly more/less enhanced across all timepoint measurements.

No consistent relationship of higher- or lower-than-average enhancement was found between the lungs and the spleen. The variation in above/below average enhancement of each organ was deemed independent of other organs.

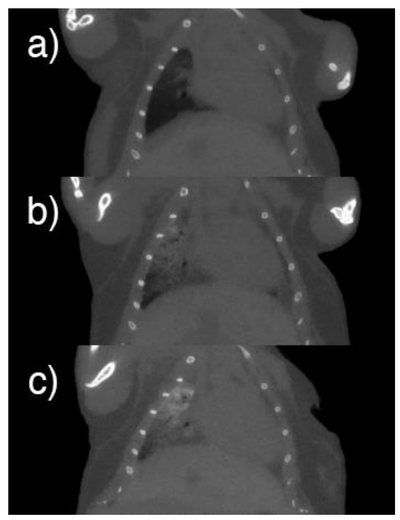

Figure 5. Images for 45 min post injection scans of 3 different mice. Differences in the enhancement of the lungs are shown. Scans are in increasing signal order with (a) showing a mouse with minimal enhancement of the lungs, (b) showing a mouse with moderate enhancement, and (c) showing a mouse with the greatest found enhancement of the lungs.

CONCLUSIONS

The novel blood-pool contrast agent was found to achieve its greatest contrast enhancement and clear from most of the body over the course of 1 day. This combination of 60% DSPC and 40% cholesterol shell with a Lipiodol core is concluded to not be an effective combination for CT imaging of the liver or vasculature. However, this CA could prove useful in animal studies where molecular imaging of the spleen with little enhancement of other tissues is desired.

REFERENCES

1. Halajian M, Kamel I, Machtaler S, Ford NL. Determining times of peak contrast enhancement of a novel computed tomography contrast agent. In: Gimi BS, Krol A, eds. *Medical Imaging 2026: Clinical and Biomedical Imaging*. SPIE; 2026:69.

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