Differences in clearance of Ferucarbotran and Ferumoxide from the liver using gradient echo MRI and T2 measurement in rat.

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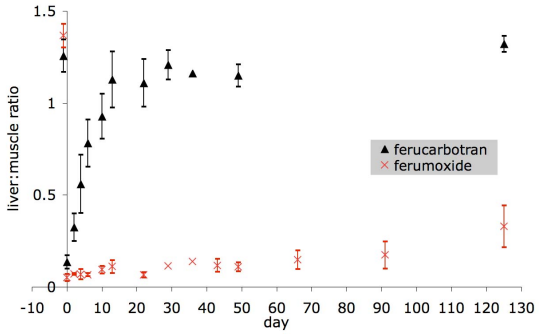
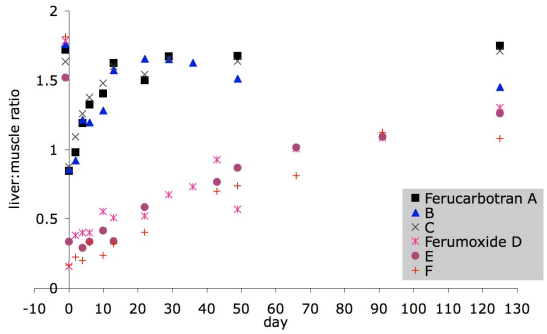
Introduction The aim of the present study is to compare the use of the two commercially available iron oxide nanoparticles, ferucarbotran (Resovist®) and ferumoxide (Feridex®), in terms of clearance from the liver. These two agents have similar properties for labeling of islet cells in terms of size, magnetic properties and toxicity, but the time to clear from the liver, on cell rejection, may vary due to the difference in coatings [1]. Although cell uptake and persistence is an important property, for cell labeling studies the efficiency of clearance on cell rejection is crucial.

Methods Sprague-Dawley rats (n=6) were injected with a solution of one of the agents in a concentration and volume similar to that used in cell labeling and transplantation [2,3]. Imaging was carried out, from day 0 to 125, using a clinical 1.5 Tesla MRI scanner (Achieva, Philips Medical System, Best, The Netherlands) with anesthetized animals positioned prone head first on a 4.7cm-diameter circular MR coil. To visualize iron oxide in the liver due to signal loss, as in the in-vivo islet transplant case, a T1 weighted fast field echo (T1w FFE) acquisition was performed over the liver volume; MR parameters were: slice thickness = 2 mm, FOV = 150 x 150 mm, TE/TR/FA = 5.1ms/500ms/50°, acquisition time = 5 min 34 s, acquired in-plane resolution = 0.3 x 0.45 mm^2, reconstructed in-plane resolution = 0.15 x 0.15 mm^2, number of scan averages (NSA) = 2. Two saturation bands with thickness of 60mm were placed above and below the imaging plane to reduce blood and motion artifacts. To calculate T2 decay, a 16 echo spin-echo acquisition was obtained with the following parameters: TEs/TR/FA = 5.9, 11.8…94.4ms/333ms/90°, slice thickness = 3 mm, FOV = 75 x 75 mm^2, acquired in-plane resolution = 0.5 x 0.65 mm^2, reconstructed in-plane resolution = 0.3 x 0.3 mm^2, number of scan averages (NSA) = 4. The second echo image of this series was also used to measure liver-to-muscle signal ratio.

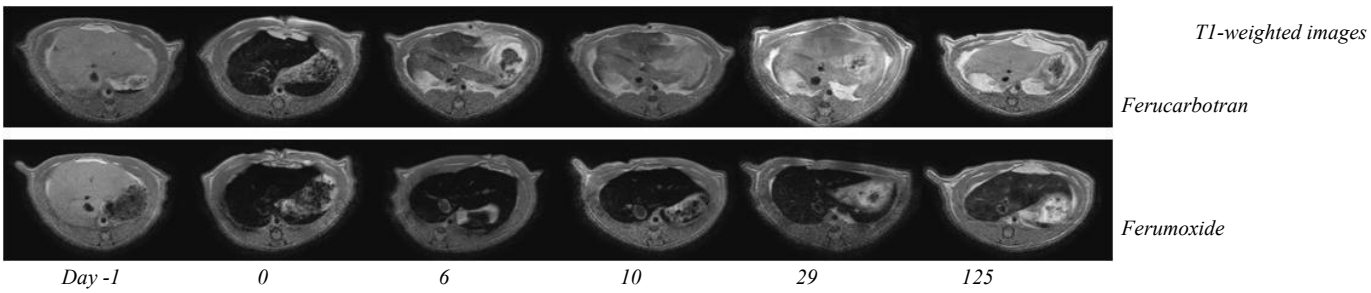
Results The graphs below the signal ratio and T2 decay evolution with time for the two contrast agents.

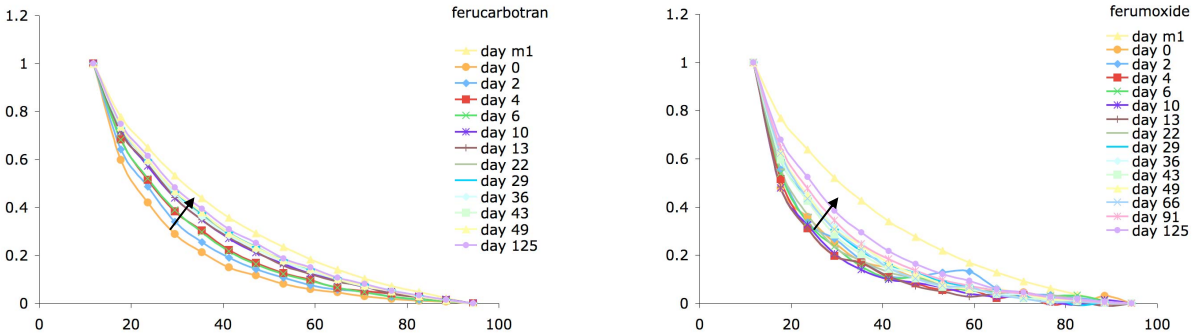


T1-weighted image, liver-to-muscle ratio with time (mean and standard deviation).



1st echo of T2-curve series, liver-to-muscle ratio with time (individual animals)





Mean T2 decay curves. Arrow indicates increasing number of days after injection.

Discussion Despite the similar size and magnetic properties of these agents, the difference in coating has a significant effect on their clearance from the liver. After 10 days, the ferucarbotran (carboxydextran coating) injected livers are back to no significant difference to normal signal levels in both T1 and T2 images (p=0.05). The T2 decay curve continues to progress over several weeks. The ferumoxide (dextran coating) injected liver shows a much slower recovery.

Conclusion The ferumoxide is not cleared efficiently from the liver, bringing into doubt its suitability for longitudinal studies of rejection of labeled graft cells. At 125 days, the liver signal and its effect on T2 decay are only half way back to baseline. Ferucarbotran would therefore be the agent of choice for cell labeling studies.

References

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