Alternative labels for visualization of pancreatic islets

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Introduction

Monitoring of transplanted pancreatic islets (PI) in vivo is an important step toward successful evaluation of transplantation outcome. Visualization of PI using MRI requires their labeling by a suitable contrast agent. Usually superparamagnetic contrast agents based on iron oxides are used, optimal results were reached using clinically approved Resovist® (ferucarbotran, carboxydextran coated ferumoxide particles) in experiments and human medicine (1). Alternatively, Feridex® (dextran-coated ferumoxide particles) in combination with a suitable transfection agent, such as poly-L-lysine (PLL) was successfully used (2). However, both contrast agents are being withdrawn from the market and there is a need for a suitable replacement – and it is a challenge to find a contrast agent possessing better magnetic properties and improved labeling efficiency. We tested maghemite nanoparticles (γ-Fe_2O_3) coated by D-mannose, PLL or poly(*N,N*-dimethylacrylamide) (PDMAAm) which were prepared by the coprecipitation method. Previous studies proved their high relaxivity and suitable physical and biological properties (3-5). The labeling efficiency was compared to commercially available Resovist® or Feridex® combined with a transfection agent (PLL). Modified surface of the new nanoparticles eliminates the need of a transfection agent.

Methods

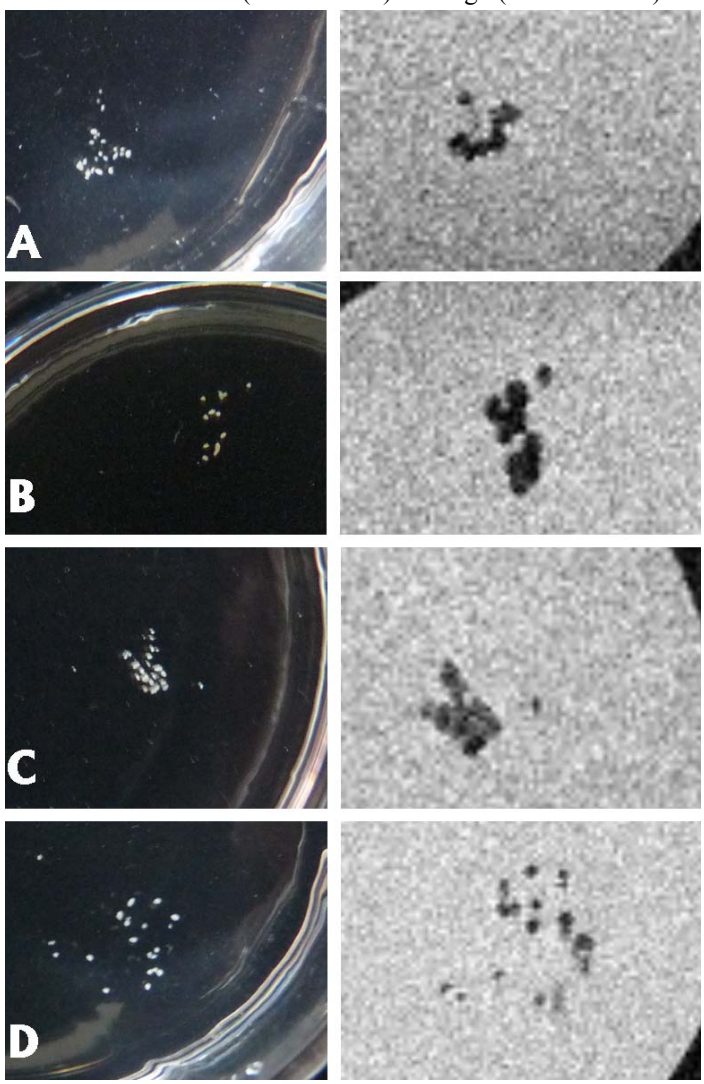
Rat pancreatic islets were isolated according to a standard protocol (6). The isolated pancreatic islets were cultured for 24 hours in CMRL-1066 medium (37°C, 5% atm. CO_2; Sigma) containing different nanoparticles at two concentrations: 140 μg Fe/mL (used standardly for Resovist®) and 25 μg Fe/mL (used in case of Feridex® in combination with PLL). PI labeled by Resovist® (140 μg Fe/mL) and Feridex® in combination with PLL (25 μg Fe/mL) were used as a control.

In vitro insulin production by labeled islets was assessed by incubation in HBSS with basal (3 mmol/liter) and high (22 mmol/liter) glucose concentrations.

The labeled islets were suspended in 4% gelatin and were measured using a 4.7 T Bruker BioSpec spectrometer equipped with a commercially available resonator coil. Standard T2W turbospin echo and T2*W gradient echo sequences were used. MR images were compared to macrophotographs.

Results

The figure shows macrophotographs (left column) and MR gradient echo images (right column) of PI labeled by Resovist (A), PLL coated (B), D-mannose coated (C), and PDMAAm coated (D) nanoparticles. Concentration of Resovist was 140 μg Fe/mL, concentration of other labels was 25 μg Fe/mL. The experiment proved that even at low concentration of iron nanoparticles in the media, the PI are sufficiently labeled to produce satisfactory contrast in the MR image. Blooming effect in case of PLL and D-mannose coated nanoparticles indicates substantially higher iron content in PI than in case of Resovist or Feridex with PLL.



The vitality (live/death cell ratio) of the labeled islets and static insulin release of the labeled islets in basal and stimulated conditions were not impaired even at higher nanoparticle concentration in the media (140 μg Fe/mL).

Conclusion

Modified iron oxide nanoparticles proved to be an alternative superparamagnetic label for detection of PI using MRI. Even at low concentrations in the media they sufficiently label the PI with no adverse effect on functionality of PI. Best results were obtained with nanoparticles coated by PLL and D-mannose.

References

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