Improved detection of pancreatic islets in vivo using double contrast

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INTRODUCTION

Transplantation of pancreatic islets is an alternative approach to the treatment of type 1 diabetes (1). Visualization of transplanted islets using magnetic resonance imaging requires labeling of islets by a contrast agent to distinguish the islets from the tissue. Usually superparamagnetic contrast agents are used; good results were obtained using commercially available Resovist® (Schering) (2) or Feridex® (Berlex) (3). Superparamagnetic contrast agents provide "negative" contrast, i.e., labeled islets are represented by hypointense areas on T_2W images. The image contrast can be improved by administration of a suitable gadolinium based contrast agent prior to the measurement. Better contrast in the MR image might enable automated evaluation of MR images and islet counting.

SUBJECTS AND METHODS

Rat pancreatic islets were isolated according to a standard protocol (2). The isolated pancreatic islets were cultured in CMRL-1066 medium (37°C, 5% atm. CO_2; Sigma) containing commercially available contrast agent Resovistt® (Schering). Labeled islets were transplanted through a portal vein to the liver of ten Wistar rats with induced diabetes. The animals underwent MRI scanning every two weeks for three months. Blood glucose level was measured weekly. As a T_1 liver contrast Gd-BOPTA (MultiHance®, Bracco) was used.

MR imaging: the animals were scanned using a 4.7 T Bruker Biospec imager and a supplied resonator coil. MRI session consisted of native images acquisition, then the contrast agent was applied through a tail vein (0.05 mL of MultiHance) and post contrast images were acquired. A standard gradient echo sequence (TE=3.4 ms, TR = 80 ms, matrix 256x256, FOV = 6 cm, slice thickness = 2 mm) was used for both native and post contrast imaging.

ImageJ software (Wayne Rasband, NIH, USA) was used for automated image evaluation and islet counting.

RESULTS

Pilot measurements showed that the liver is evenly perfused by the contrast agent approximately within 30 minutes. Signal decrease caused by washing out of the contrast was visible approximately 90 minutes post injection. Therefore, there is a fairly long acquisition window for image acquisition and we acquired images usually 30 – 60 minutes post injection.

Comparison of native and post contrast MR images of the rat liver with transplanted pancreatic islets can be seen on figures A and B.

Normal blood glucose levels were reached after 1 week after islet transplantation.

DISCUSSION AND CONCLUSION

Our results demonstrate that in vivo detection of pancreatic islets labeled by iron oxide nanoparticles can be significantly improved by application of a suitable T_1 contrast prior to MR imaging. Superparamagnetic nanoparticles have strong T_2* effect and negligible T_1 effect, therefore they ensure hypointense signal in the vicinity of the islets even on strongly T_1-weighted images. Signal enhancement of the liver tissue therefore improves their detection and delineation. However, care should be paid to setting of sequence parameters to highlight both positive and negative contrasts.

Although reliability of an automated procedure for detection and counting of particles (labeled islets) was significantly improved, the procedure still requires thorough manual control.

As normal glucose level was reached after 1 week, which is in accordance with published data (2), and was maintained though the whole three-month experiment, we suppose that application of MultiHance during MR imaging probably has no long-term impact on function of pancreatic islet.

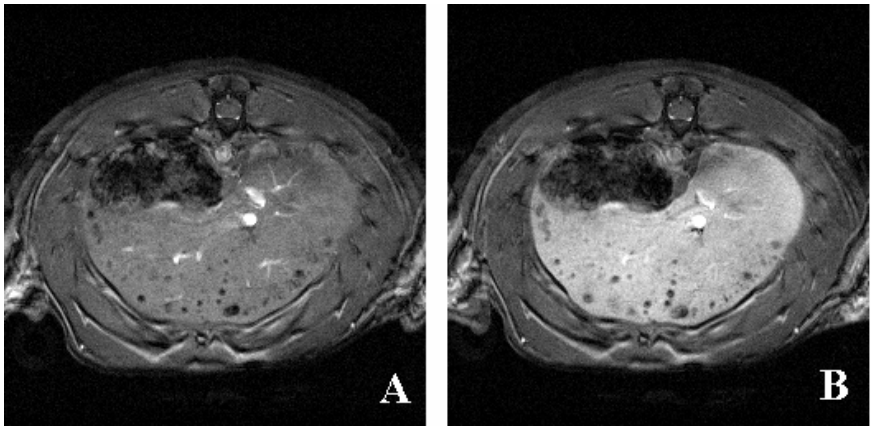

Fig.: Native (A) and post contrast (B) MR image of the rat liver with transplanted labeled pancreatic islets.

References

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