MRI of pancreatic islets labeled by Dynabeads

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Introduction

Transplantation of pancreatic islets is an alternative approach to the treatment of type 1 diabetes (1). Transplanted islets labeled by the superparamagnetic contrast agent Resovist® can be easily visualized by MR as reported previously (2). The long staining time (48 hours) and nonspecificity could be significant disadvantages of this technique in a possible clinical application. The aim of this study was to test a contrast agent based on beads coated by specific anti-beta cell antibodies for imaging transplanted pancreatic islets both in vitro and in vivo experiments.

Subjects and Methods

Pancreatic islets were isolated according to a standard protocol (3). The isolated pancreatic islets were cultured in CMRL-1066 medium (37°C, 5% atm. CO_2; Sigma) containing Dynabeads M-450 (Dynal Biotech, UK) for two hours. Dynabeads are paramagnetic particles coated with specific antibodies (mouse IgG betacell surface-specific antibody K14D10 and secondary antibody anti-mouse IgG) (4). One thousand purified and labeled islets were transplanted into the liver through the portal vein. Then the portal vein was ligated, and after 5 minutes the animal was exsanguinated and liver explanted from the abdominal cavity and examined in vitro by MR. (n=5). In vivo experiments were performed on 8 healthy Lewis rats that underwent syngeneic islet transplantation. Six untreated rats were measured as controls (no transplanted or labeled islets). All animals were scanned weekly for two months after transplantation by a 4.7 T Bruker Biospec spectrometer equipped with a home-made surface (in vitro study) or resonator (in vivo study) coil. We used a gradient echo sequence, TR = 80ms, TE = 3.4 ms, slice thickness = 2 mm, slice separation = 3 mm, number of slices = 8, number of averaging = 16, FOV = 6 cm and matrix = 256x256.

Results

Labeled pancreatic islets were clearly visualized in all the examined liver samples as hypointense spots (size 0.1-3mm^2) on MR images in the in vitro experiment (Figure 1) Similarly to the in vitro experiment, labeled islets were also visualized in vivo in all animals at each examination. The observed hypointense regions (size 0.1-3mm^2) did not noticeably change in either their shape or their size; they were irregulary distributed throughout the whole liver and remained in the same positions during the entire monitored period (Figure 2ab).

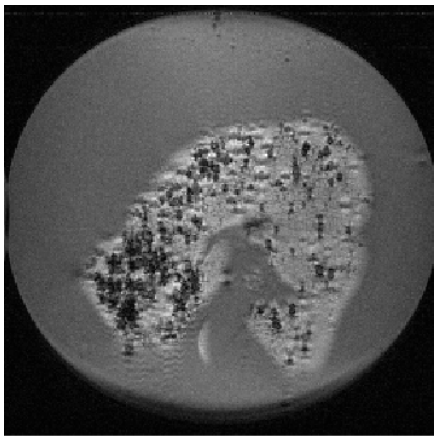

Figure 1: T2*-weighted MR image of a rat liver with 1000 transplanted islets measured in vitro.

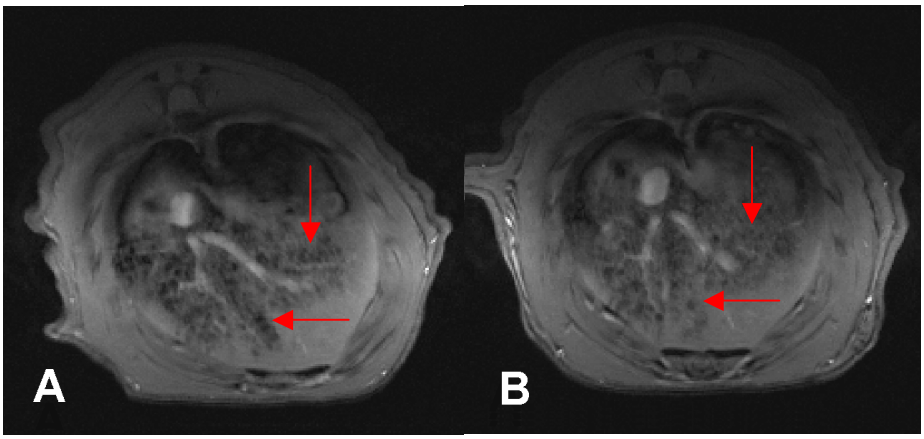

Figure 2: T2*-weighted MR image of a rat liver with 1000 transplanted islets measured in vivo 1 week (a) and 4 weeks (b) after transplantation of labeled pancreatic islets (arrows point to islets as an example).

Discussion and Conclusions

Our results demonstrate that pancreatic islets labeled by Dynabeads can be visualized by MR both in vitro and in vivo. Islets are shown as hypointense spots in the liver on T2*W MR images. The Staining time was significantly shorter than with the use of a nonspecific contrast agent (Resovist®) and did not exceed 2 hours. The use of beads covered with antibodies against beta cells increased the specificity of the method. We conclude that the presented protocol can be used for islet imaging after transplantation. Further study is needed to evaluate the secreting capacity of labeled islets and their ability to induce normoglycaemia in diabetic recipients.

References

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