Clinical field-strength MRI of transplanted pancreatic islets in a large animal model

Z. Medarova[1], P. Vallabhajosyula[2], B. Jenkins[1], N. Evgenov[1], A. Hirakata[2], K. Yamada[2], D. Sachs[2], and A. Moore[1]

[1]Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, United States, [2]Transplantation Biology research Center, Massachusetts General Hospital, Charlestown, MA, United States

Background

Clinical magnetic resonance imaging (MRI), as compared to small animal MRI, is limited by the signal-to-noise ratio (SNR), susceptibility, and resolution associated with relatively low field strengths and using larger fields of view. Clinical MRI of humans typically images a cube (voxel) of tissue 1x1x1 millimeter, whereas voxels imaged with MR microscopy of small animals can be 10,000 times smaller: 50x50x50 micrometers. The loss in SNR and susceptibility when transitioning from 4.7T to 1.5T can be 2-3-fold. Therefore, high-resolution MRI studies in small animals are typically associated with high magnetic field strengths. Combined with sensitive superparamagnetic iron oxide (SPIO) contrast agents, high field small animal MRI can produce enough susceptibility to detect individual SPIO-labeled cells in vivo (1,2).

Previously, we have developed a method for the noninvasive MR imaging at the 4.7T field strength of human pancreatic islets labeled with superparamagnetic iron oxides and transplanted into mice (3-5). For translation of this study into clinic it is necessary to adopt clinical strength magnet in combination with large animal model. In our present study, we utilized the 1.5T scanner for the detection of transplanted islets in a non-human primate model. Pancreatic islets are small structures (~ 200μm in diameter) and, therefore, their visualization by MRI at 1.5T and using fields of view suitable for abdominal imaging of non-human primates represents a novel and challenging proposition. Considering the vast differential in the difficulties associated with detecting pancreatic islets at high field strengths in small animals vs. clinical field strengths in large animals, these studies represent an essential intermediate step before the transition from experimental to clinical applications.

Methods and Materials

Islet labeling: Baboon islets were incubated overnight with the FDA-approved commercially available agent, Feridex (200μg Fe/ml), which is clinically used for liver imaging.

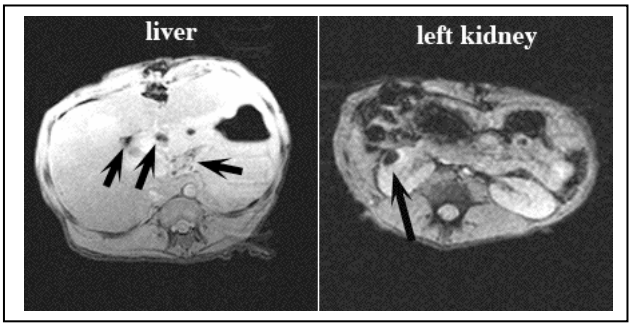
Islet transplantation: Autologous, Feridex-labeled baboon islets were transplanted into both the liver, via intra-portal infusion, and underneath the left renal capsule.

Imaging: In vivo MR imaging was performed before and after transplantation using a 1.5T Siemens Trio magnet equipped with a 6 channel body matrix coil and a spine-array coil. The imaging parameters were as follows:

Liver:

a) (with respiratory gating)- TR/TE = 100/2.3-29.3 ms, slice thickness 3 mm, FoV = 200 x 200 mm^2, matrix size 192 x 192, flip angle = 25°, and in plane resolution 1 x 1 mm^2.

b) (with navigator)- TR/TE = 2000/4.76-61.3 ms, slice thickness 3 mm, FoV = 200 x 200 mm^2, matrix size 256 x 256, flip angle = 70°, and in plane resolution 0.78 x 0.78 mm^2.



Kidney:

a) TR/TE=200/2.3-29.3 ms, slice thickness 3 mm, FoV = 180 x 180 mm^2, matrix size 192 x 192, flip angle = 25°, and in plane resolution 0.9 x 0.9 mm^2.

b) (with navigator)- TR/TE = 2000/4.76-61.3 ms, slice thickness 3 mm, FoV = 180 x 180 mm^2, matrix size 256 x 256, flip angle = 70°, and in plane resolution 0.7 x 0.7 mm^2.

Results

Using the specified MR imaging sequences, pancreatic islets labeled with Feridex and transplanted into the livers of nonhuman primates could be easily visualized against the background of the liver parenchyma as signal voids along the hepatic blood vessels. Islets in left kidney appeared as a pocket of signal loss over the capsule (not seen in right kidney) (Fig 1).

Summary

This study describes for the first time the in vivo detection of transplanted pancreatic islets using clinical field strength MRI in a large animal model. The challenges associated with the visualization of structures the size of islets (~200μm in diameter) are unprecedented in the described imaging context. These experiments represent an essential intermediate step before translating MR imaging of islet transplantation from experimental to clinical applications.

References

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