Monitoring of transplanted pancreatic islets in humans by MRI

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Introduction

Labeling of pancreatic islets (PI) with superparamagnetic iron oxide (SPIO) nanoparticles enables their direct posttransplant visualization by magnetic resonance (MR) as hypointense areas on T2/T2* weighted images [1]. It might help to study the posttransplant islet distribution and survival. We tracked SPIO labeled PI in type-1 diabetic recipients and quantified the islet loss in liver tissue by MR imaging during 6 months after transplantation.

Subjects and Methods

Freshly isolated PI (280 - 480 ths islet equivalents) were in vitro labeled in CMRL – Miami medium supplemented with a clinically approved MR contrast agent ferucarbotran (5 μL/mL) for 6-44 hours), washed to remove free ferucarbotran and then transplanted into the portal vein in 10 C-peptide negative recipients (8 nonuremic, 2 after kidney transplants, 1 after pancreas transplants). The liver imaging was performed on a 3T Trio TIM MR system (Siemens Healthcare, Germany) using a standard and fully refocused steady-state free precession (SSFP) gradient-echo sequences with a resolution of 1.3x1.3x2.5 mm^3 on days 1, 7, 14, 28 and 168 after PI transplantation. The images were acquired in transversal and coronal planes within the breath hold (20 sec). Hypointense islet spots and their area were counted and outlined manually by an investigator using ImageJ software (NIH, USA). Their total number 1 day post transplant was rated as 100% and subsequent measurements of signal loss regions were recalculated as relative numbers.

Results

In all recipients, C-peptide levels > 0.5 pmol/ml and near-normal HbA1c values were achieved with insulin dose reduction of 50-80%. Regions of signal loss attributed to transplanted islets were detected in MR images in all recipients immediately after transplantation, confirming its technical success (Figure 1). During the first week after transplantation we observed a dramatic decrease of number of spots (44%). and area of spots related to PI (46%). Then the decline slowed down (between 7-168 days: 23% (number of spots), 38% (area of spots)). Data are summarized in Table 1.

Discussion and Conclusions

MR confirmed the technical success of PI transplantation in all recipients and enabled their posttransplant PI detection. Function of transplanted PI was confirmed by C-peptide production. A dramatic loss of hypointense spots occurred in the 1st week suggesting a wash out of free SPIO particles and impaired PI or their early destruction. Then the number of PI spots and their area stabilized. It is in accordance with data obtained in an animal model [2] and supports the hypothesis that in the first few days (repeatedly described as high-risk period for islet engraftment) there is an erratic response to the transplanted tissue. Our data suggest that post-transplant MR monitoring might be of importance for assessment of the islet fate following clinical transplantation.

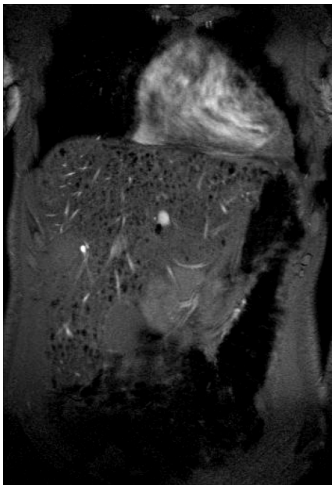

Figure 1: Gradient-echo image of patient one day after transplantation. Hypointense area in liver tissue is attributed to the transplanted pancreatic islets.

Decline in regional signal loss					
Days following the first transplantation	1	7	14	28	168
Number of spots [%]	100	55.8±3.9*	46.3±8.0	45.8±5.8	32.8±7.8
Area of spots [%]	100	54.3±7.7*	38.7±8.2	33.2±5.8	16.0±4.2

Table 1. Relative area of signal loss for detected transplanted PI during the six months. A statistically significant decrease in both number of spots and their area, compared to the initial values in day 1, was observed at 7 days after transplantation. * P < 0.01 day 1 versus day 7; Wilcocson paired test.

References
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2. Jirak D, Kriz J, Strzelecki M, et al. Monitoring the survival of islet transplants by MRI using a novel technique for their automated detection and quantification. MAGMA 2009; 22: 257.

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