Monitoring of the blood supply to artificial cavity used as a site for pancreatic islet transplantation

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Introduction

Pancreatic islet (PI) transplantation has been exploited as an alternative treatment of Type-1 diabetes. More than 50% of PIs are destroyed in the first two days after transplantation into the portal vein [1]. Therefore, to improve transplantation outcome, artificially created sites for islet transplantation have gained attention in the scientific community. The adequate vascular network is crucial for PI engraftment. Therefore the aim of our study was to evaluate the blood supply to the internal space of artificially created cavities and to determine the optimal time for cell transplantation in a preclinical rat model.

Subjects and Methods

Two polymeric meshes shaped in rounded scaffolds were implanted subcutaneously or into the greater omentum of Brown-Norway female rats (n = 18); 180–220 g; Charles River, Germany). On the day of implantation as well as 1, 3, and 4 weeks later, anesthetized animals (1.5% Isoflurane; Baxter, Belgium) were scanned at a 4.7 T Bruker Biospec MR scanner (Bruker BioSpin MRI, Germany) equipped with a resonator coil. To assess neovascularization at the transplantation site, we analyzed the changes of the signal intensity observed within selected target areas after intravascular contrast agent Vasovist^{TM} administration (0.05 ml/100 g, Bayer Schering Pharma, Germany) by dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI). For the DCE-MRI, a 3-dimensional gradient echo sequence was used with the following parameters: echo time/repetition time (TE/TR) 3.1/10 ms (32 repetitions), matrix 256x128 pixels, resolution 0.243x0.469x0.422 mm^3, evolution delay 5.0 s, target volume was covered by 64 layers. After the 10th cycle, the contrast agent (60 µl) was promptly injected into the lateral tail vein. The regions of interest were manually outlined and mean pixel intensity within each target structure (omental device, subcutaneous device, kidney) was calculated (ImageJ software, NIH, USA) for every cycle. The average signal intensity during the first 10 cycles was considered the basal level. The average signal intensity during the last 10 cycles (plateau phase) was considered to be the contrast-enhanced level. To minimize the influence of variability in contrast agent application, all outcomes measured in the implanted devices were normalized to the signal intensity of kidney. All protocols were approved by the Ethical Committee of the Institute for Clinical and Experimental Medicine and the experiments were carried out in accordance with the European Communities Council Directive (86/609/EEC).

Results

The implanted polymeric devices have not caused any adverse effect in rats nor any image artifacts. One week after the implantation, the connective tissue had adequately penetrated and covered the porous devices. The penetration of the contrast agent was detected by the increase in signal intensity within implanted devices. On day of implantation of the device, no signal due to the contrast agent was detected in all devices. However, over the following weeks, there was an increase in signal detection within the omental device to 34% (week 1), 21% (week 3), and 14% (week 4) of that measured within the kidney. Within the subcutaneously implanted devices there was an increase in signal detection up to 11% (week 1), 10% (week 3), and 7% (week 4) of that detected in the kidney. Macroscopic view on cell pouch formation reveal that the vessel network was well established one week after implantation in tissue surrounding artificial devices covered by both greater omentum and the subcutaneous tissue. In microscopic view, compact connective tissue was observed in samples excised one week after implantation. Microscopy also confirmed that only in omentum four weeks after the device implantation multiple vessels of various diameters located on the external surface of the scaffold were observed.

Discussion and Conclusions

MR results indicate that artificial device implanted into greater omentum possesses superior blood supply for the transplanted cells and it is in accordance with the microscopic/macroscopic findings. Blood supply is relatively rich one week after implantation and dramatically decreased in time. Therefore preferable artificially created site for PI transplantation seems to be greater omentum and the optimal time for cell transplantation is one week after scaffold implantation.

References

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