Dynamic Contrast-Enhanced Magnetic Resonance Imaging as a Tool to Monitor the Blood Supply to an Artificial Cavity Used as a Site for Islet Transplantation in Rats

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ABSTRACT

Background. The transplantation of islets of Langerhans isolated from one donor pancreas can rarely release a diabetic recipient from insulin injections. The major reason is the destruction of 50%–60% of the transplanted tissue, which proceeds typically within a few hours after the insertion of the islets into the portal vein. Therefore, several groups have focused on development of an artificial site for islet transplantation. The main aim of the present study was to test the efficacy of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) to evaluate the blood supply feeding the artificially created cavities for islet transplantation.

Methods. Two rounded devices were implanted: one device subcutaneously and the second one into the greater omentum of each animal. On the day of implantation as well as 1, 3, and 4 weeks later, we quickly injected the vascular specific MR contrast agent Vasovist (0.05 mL/100 g) intravenously. Penetration of the contrast agent was monitored by DCE-MRI. The influence of the contrast agent on the signal intensity observed within selected target areas was calculated with the use of ImageJ software.

Results. The penetration of the contrast agent was detected by the increase in signal intensity within implanted devices. The signal increase caused by the contrast compound was normalized to kidney tissue. 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%, 21%, and 14% of that of the kidney. Within the subcutaneously implanted devices there was an increase in signal detection up to 11%, 10%, and 7% of that detected in the kidney.

Conclusions. The optimal time for transplantation of pancreatic islets into our omental device was 1 week after implantation of the scaffold. Also, the blood supply feeding the subcutaneous devices was regarded to be inadequate.

THE transplantation of pancreatic islets into the hepatic portal vein is not an optimal procedure owing to inadequate engraftment and shortened graft survival.[1–4] Therefore, artificially created sites for islet transplantation have gained attention in the scientific community.[5–7] We tested an artificial cavity created using a polymer composite implanted simultaneously into the greater omentum and subskin of diabetic rats. The outcomes of islet transplanta-

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tion using these artificial devices were deemed to be promising but required further optimization.[6,8] Taking into consideration the extremely high oxygen demand of islets, we proposed that the initial limited vascularization of the transplantation site was crucial for failure of islet engraftment. Several groups, including our own, have considered a period of 4 weeks between scaffold implantation and islet transplantation to be adequate for cells engraftment.[5–7] This required time is deemed to be necessary to permit proper wound healing allowing subsidance of the surgically induced inflammation. Our previously published study focused on changes in the macroscopic vascular network surrounding the scaffold over time.[8] Magnetic resonance imaging (MRI) and MRI angiography indicated that fibrous tissue ingrowth with accompanying large vessels was completed at 1 week after scaffold implantation.[8] However, that study did not specifically characterize the blood supply that was contained inside the artificially created transplantation site. Nonetheless, from the quality of the vascular network surrounding the scaffold, we concluded that the tissue perfusion declined over 5 weeks after implantation.[8] We needed a technique to monitor the blood supply within the tissue. Therefore, we considered contrast agent extravasation monitoring by dynamic contrast-enhanced (DCE) MRI, because it had been previously used clinically to characterize tumor neoangiogenesis,[9,10] as well as to monitor revascularization of transplanted pancreatic islets.[11] We hypothesized that DCE-MRI could allow us to assess the blood supply and extravasation into the device and therefore identify the optimal timing of islet transplantation.[12] Thus, the goal of the present experimental study was to monitor the penetration of an intravenously injected contrast agent into tissue in direct contact with the implanted devices.

METHODS

Rounded scaffolds created from a polymeric composite mesh were implanted in male Brown Norway rats (180–220 g; Charles River,

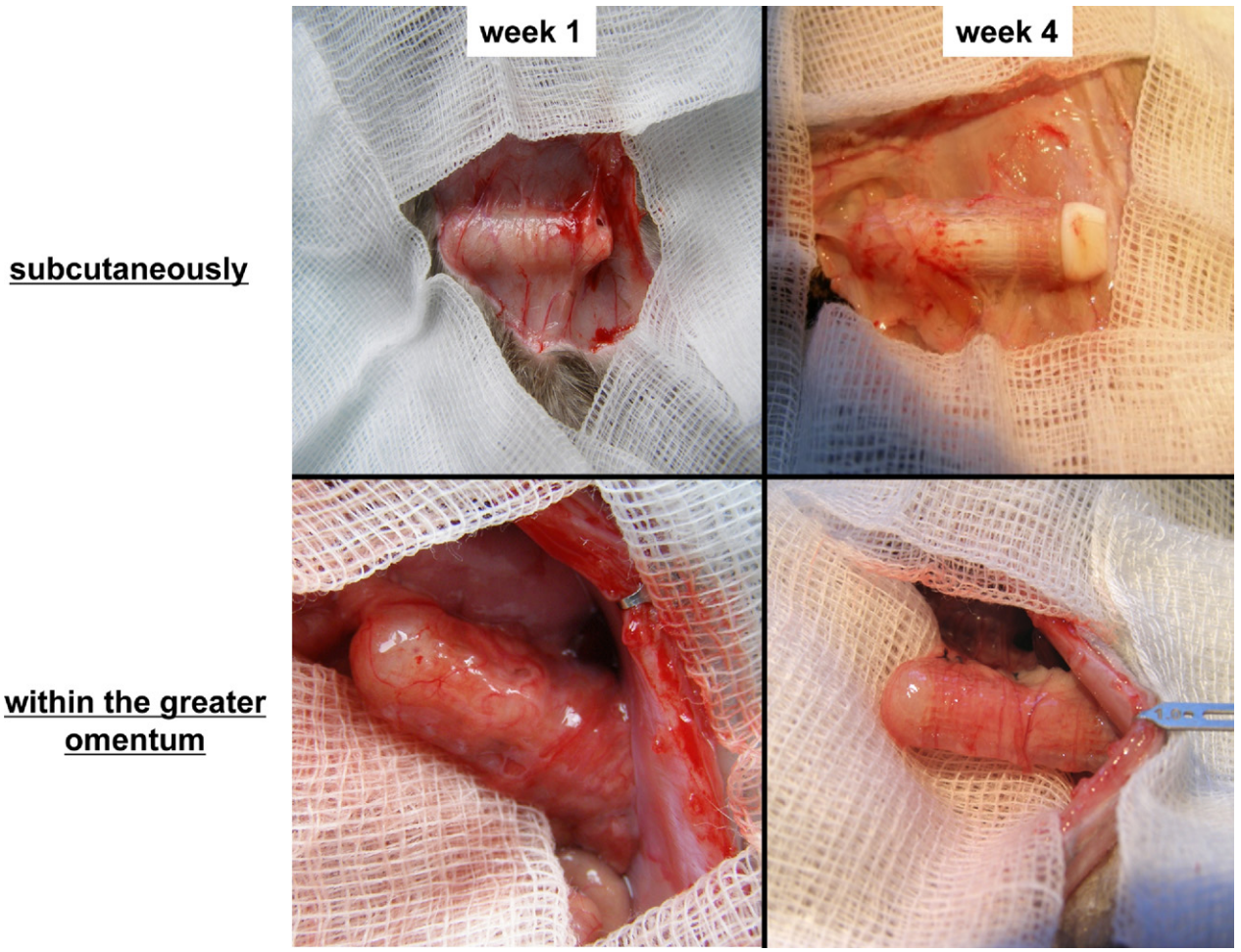

Fig 1. Macroscopic view on cell pouch formation: The vessel network looked well established after 1 week and then stable in tissue surrounding artificial devices covered by greater omentum. In contrast, the subcutaneous tissue surrounding the device was well vascularized in 1 week, but vasculature disappeared later.