Intraportal Islet Transplantation Assessed by Dynamic Contrast Enhanced Magnetic Resonance Imaging

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Introduction

Pancreatic islet transplantation can provide short-term insulin independence and near normal glucose tolerance in patients with type 1 diabetes mellitus. However, islet cell mass decreases dramatically over 5 years and insulin independence is not maintained. A number of clinical (Toso 2008) and animal research studies have demonstrated the ability of MRI to readily visualize transplanted islets. Since islets are avascular immediately following transplantation, angiogenesis to support islet survival and function is critical. Non-invasive visualization of angiogenesis using dynamic contrast enhanced (DCE) MRI, has great potential clinical applicability for assessing revascularization of intraportal transplanted islets. The data from our study support this hypothesis.

Materials and Methods

Murine islets were incubated with superparamagnetic iron oxide (Feridex) for 18 hrs. 800 syngeneic islets/recipient were injected into the right lobe of the liver. MRI of the liver was conducted at post transplant days (POD) 3, 7, 14, and 28 on an 11.7T scanner (n=6/time). DCE was performed by pre-contrast T1 MRI, followed by a bolus injection of gadolinium contrast agent (Gd-DTPA) (0.8 mmol/kg body weight). DCE MRI captured images every 32sec for 30 min. Analysis utilized the Tofts model and DCE curves were quantified for area under the curve (AUC). Immunohistochemical confirmation was undertaken for insulin and von Willebrand Factor (vWF) and Prussian blue staining for iron.

Results

Iron-labeled Islets were readily visualized on T2 in the right hepatic lobe. DCE demonstrated significantly increased contrast enhancement in the right liver at POD 7 and POD 28 as compared to POD 3 (Fig 1A). Prussian blue staining showed some iron containing cells (Fig. 1B). Immunohistochemistry for insulin demonstrated islet presence after intraportal implantation. Staining for new vessels using vWF at POD 7 revealed a small number of new vessels at the periphery of the islets (Fig. 1B, arrows).

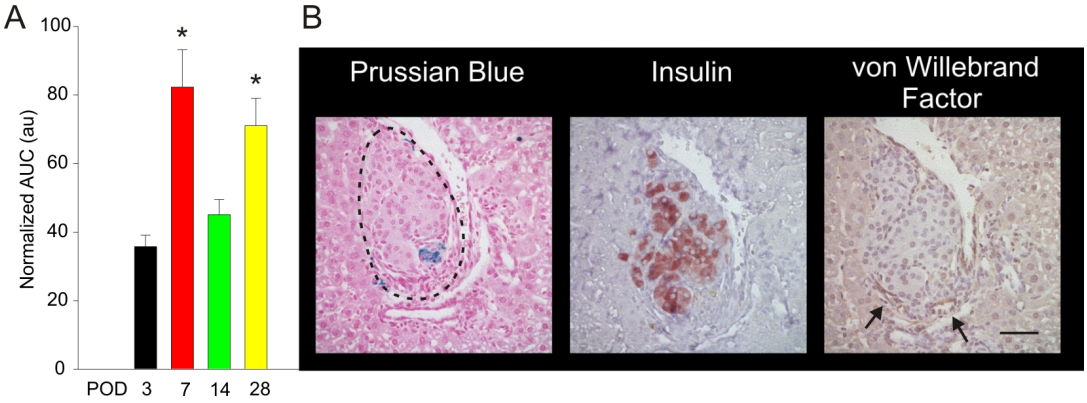

Figure 1: A) AUC analysis of DCE curves demonstrated an increase in contrast extravasation within the islet transplanted liver at POD 7 and 28 (*p<0.05). **B)** Iron staining showed labeled islets (dotted line) that also positively stained for insulin. New vessel formation (vWF; arrows) could be seen at the periphery of the islets.

Conclusions

Contrast enhancement based on DCE MRI in the transplanted liver lobe may reflect peri-islet neovascularization. Future correlation of vascularization with DCE results should provide a definitive method for non-invasive assessment of islet health after transplantation. Thus, DCE MRI may be useful in monitoring vascularization of intrahepatic islet grafts in a clinical setting.

References

Toso C., Vallee J.-P., Morel P., et al. (2008) Clinical Magnetic Resonance Imaging of Pancreatic Islet Grafts After Iron Nanoparticle Labeling. Am J Transpl. 8:701-706

Acknowledgements

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