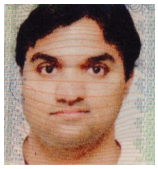
Noninvasive in vivo comparison of the vascular response to syngeneic and xenogeneic islet Transplantation



Krishnan R, Arora R, Lamb M, Liang O, White SM, Moy A, Storrs R, Dorian R, King S, Foster C, Botvinick E., Choi B., Lakey JRT
Department of Surgery, University of California Irvine, California, United States. (rkrishn1@uci.edu)

INTRODUCTION AND OBJECTIVES

Xenotransplantion provides a possible solution to human islet donor scarcity. However, the rapid, immune-mediated destruction of transplanted islets in the absence of prolonged immunosuppression makes it currently unviable. Studies have demonstrated that biomaterial encapsulation of xenograft islets prolongs their survival and obviates the need for immunosuppression. However with encapsulation, islet survival is compromised due to insufficient oxygen delivery via the microcirculation. Thus, a brisk vascular response is vital to reduce the risk of hypoxia in the transplanted islets. We aim to compare the responses to isograft and xenograft islets by employing a combination of the mouse dorsal window-chamber model and Wide-field Functional Imaging (WiFI) and Laser Speckle Imaging (LSI).

MATERIALS AND METHODS

Dorsal window chambers (Fig 1.) were installed on C57BL/6 albino mice. The implants were placed in intimate contact with the underside of the dermis of the opposing skin, within the viewing port of the model.

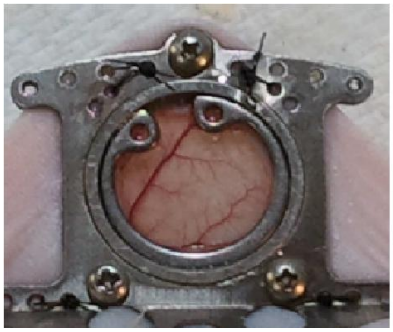


Fig 1. Lateral view of the dorsal window chamber

We studied the host vascular response to the introduction of a high guluronate alginate sheet containing either syngeneic islets isolated from C57Bl/6 mice or one containing xenogeneic islets isolated from 3 week old Yorkshire pigs after one week of in-vivo maturation using protocols developed in our laboratory. Two modes of WiFI (Moy AJ et al, 2011) were used to monitor hemodynamics over the ensuing 7-day period.

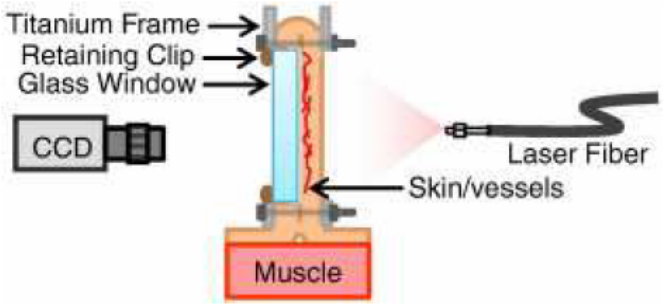


Fig 2. Schematic diagram of the imaging setup

Speckle flow index maps obtained by processing images obtained after transilluminating the window chamber with a 633 nM helium-neon laser(Fig 2.) enable observation of longitudinal changes in the rate of blood flow. Multispectral imaging of the chamber after transillumination with bright light and allowing the light to pass through a series of specific filters enables mapping of longitudinal changes in hemoglobin oxygen saturation in the peri-implant vasculature.

RESULTS AND DISCUSSIONS

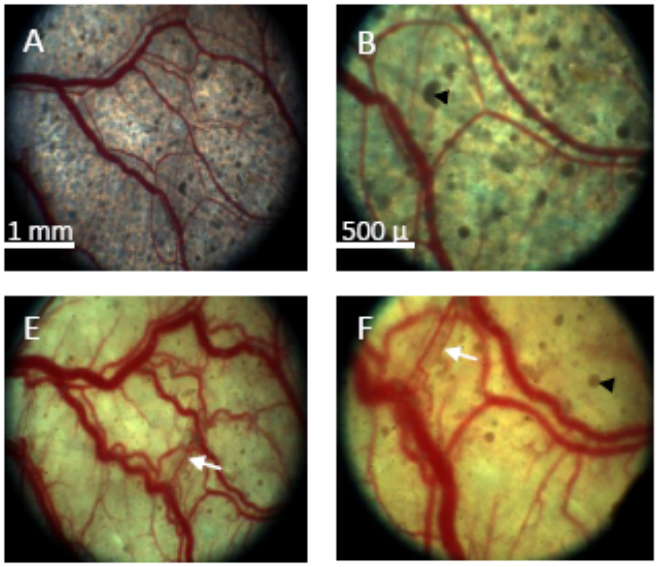


Fig 3. Vascular response observed after transplantation of alginate encapsulated syngeneic islets in the mouse dorsal window chamber

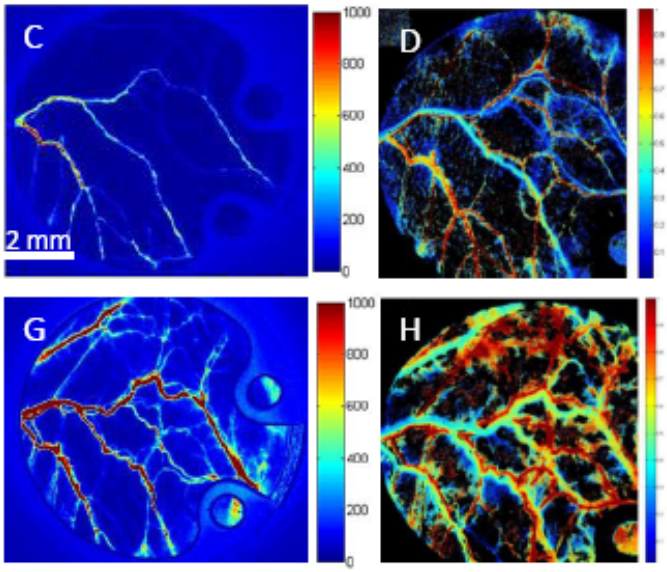


Fig 4. Hemodynamic changes observed after transplantation of alginate encapsulated syngeneic islets in the mouse dorsal window chamber

Our data demonstrates that the dorsal window chamber enables longitudinal implant monitoring and easy comparison of the vascular response to transplanted islets isolated from various donors over a one week period. Vascular changes that are readily noted include arteriolar, venular and venous dilatation and peri-implant neovascularization(Fig. 3 E,F, & Fig 5. E,F).

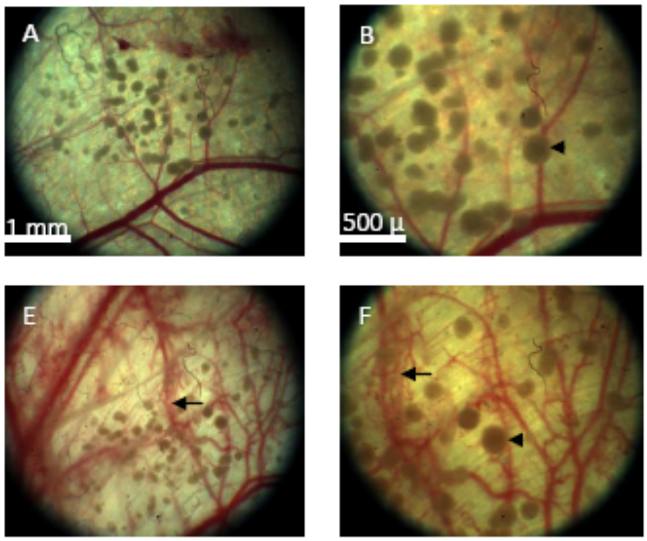


Fig 5. Vascular response observed after transplantation of alginate encapsulated xenogeneic porcine islets in the mouse dorsal window chamber

Peri-implant neovascularization, while noted in both groups was significantly more in the porcine islet group(Fig 5F). We hypothesize that this is presumably due to a greater metabolic demand by the larger porcine islets when compared to the much smaller murine islets.

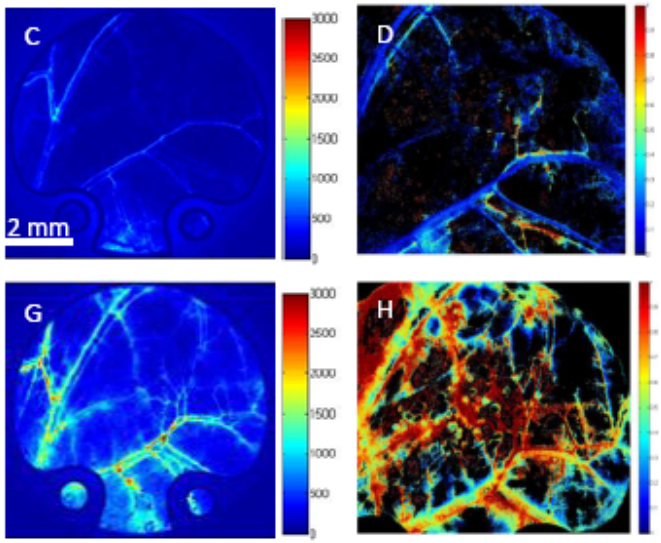


Fig 6. Hemodynamic changes observed after transplantation of alginate encapsulated xenogeneic porcine islets in the mouse dorsal window chamber

A 2-3 fold increase in the relative rate of blood flow(Fig.4C,G and Fig.6 C,G) and a two fold increase in hemoglobin oxygen saturation (Fig 4D,H and Fig 6D,H.) of the peri-implant vasculature can also be observed.

CONCLUSIONS:

The dorsal window model can conveniently be employed to study the vascular response to implanted islets and biomaterial devices. Future experiments, will study whether this phenomenon favorably affects islet viability and function for up to two weeks post-transplantation and quantify the response using algorithms being developed in our laboratory.

REFERENCES:

Moy AJ, et al. (2011) *Wide-field functional imaging of blood flow and hemoglobin oxygen saturation in the rodent dorsal window chamber*. Microvasc Res.82(3):199-209.