EFFECT OF HEAT TRANSFER ON THE EFFICACY OF HYPOTHERMIC COLD STORAGE METHODS

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ABSTRACT

One of the major impediments in clinical pancreatic islet transplantation is the lack of current agreement on optimal conditions for pancreas preservation before islet isolation. To retard cellular metabolism and reduce oxygen consumption, islet cells are typically maintained at a low temperature during preservation. However, cellular ischemic injury that results from such a cold storage method reduces the islet yield and viability and the accompanying chances of a successful transplant. The Two-Layer Method (TLM) of organ preservation, a protocol credited to Kuroda *et al.* at Kobe University, is reported as effective in preventing the adverse effects of both cold and warm ischemia and in increasing the viability of islet cells. Although it is generally believed that the TLM has superior functional efficacy over other methods (like simple cold storage with either University of Wisconsin (UW) solution or perfluorocarbon (PFC) alone), the fundamental basis for the putative efficacy of TLM still remains unexplained. This study hypothesizes that the TLM conveys salutary cell preservation due to favorable heat transfer between the pancreas tissues and the participating fluids viz. UW solution and PFC. In this work, experimental investigations of the heat transfer mechanism between the fluids and pancreata are studied. Initial experimental data for simple storage in PFC and UW solutions alone have been generated. It is found that there is a 33% difference in temperature (ΔT) between the two methods at the end of 6 minutes and this ΔT is found to exist for an extended period of time (till 1.5 hrs). These data provide reference values for in vitro experimentation of the Two-Layer Method.

INTRODUCTION

In TLM the pancreas is secured at the interface between two immiscible liquids viz. the University of Wisconsin (UW) solution-containing physiological tissue perfusion solution and a non-electrolyte-containing neat perfluorochemical (Perfluorodecalin) liquid [Kuroda et. al.,1988]. On the other hand, in simple storage method of pancreata preservation, the tissue is entirely submerged in either one of the preservation solutions. PFC is a high density (specific gravity ~ 2.0), non-electrolyte having low specific heat and thermal conductivity (Cp=1050 J/Kg.K; K=0.057 W/m.k). The physical and thermal properties of UW solution closely resemble that of water (Specific Gravity ~1.0, Cp=4018 J/Kg.K, K=0.57 W/m.k). Most available literature on TLM compares the functional efficacy of the TLM over simple storage in UW and PFC solutions independently based on graft survival rates post transplant [Kuroda et. al., 1993; Hiraoka et. al., 2001]. As a benchmark study, experimental evaluation of the cooling process in UW and PFC solutions independently using a tissue surrogate (agarose gelatin), was performed.

METHODOLOGY

Experimental Procedure: Agarose gelatin is used as the pancreas tissue surrogate as the thermal and physical properties of agarose gelatin resemble closely to that of actual pancreatic tissue. The mass of tissue surrogate is maintained constant for all experiments. T type insulated thermocouples are used in conjunction with a data acquisition system (National Instruments) to obtain the spatial and temporal temperature profiles. The temperature profiles are recorded in units of volts and subsequently converted to °C (degree Celsius) using a linear calibration curve. The thermocouples are calibrated before each experiment to eliminate or minimize any zero shift errors. The tissue surrogate is placed in a container filled with a fixed volume of either of the solutions. Thermocouples are placed at equal intervals along the radius of the surrogate as shown in Figure 1. The symmetry of the experimental model was employed to generate data points on either side of the axis. The system is cooled at a uniform rate from the initial condition to steady state using a water bath (Fischer Scientific).

Boundary and Initial conditions: The outer wall of the container is always maintained at a uniform temperature of 4 °C. The top surface of the container is kept insulated. The tissue surrogate is initially maintained at a steady state temperature of 37 °C. The solution (UW/PFC) is kept at 23 °C at the start of the experiment.

RESULTS

The viscosities of UW and PFC solutions at 25 °C have been determined experimentally in this work and the data is as shown in Figure 2. The viscosity of UW solution was found to be 3.5 cP. It exhibits a completely Newtonian behavior. PFC solution, on the other hand, shows a highly Non-Newtonian behavior and has an infinite shear rate viscosity of 11.9 cP.

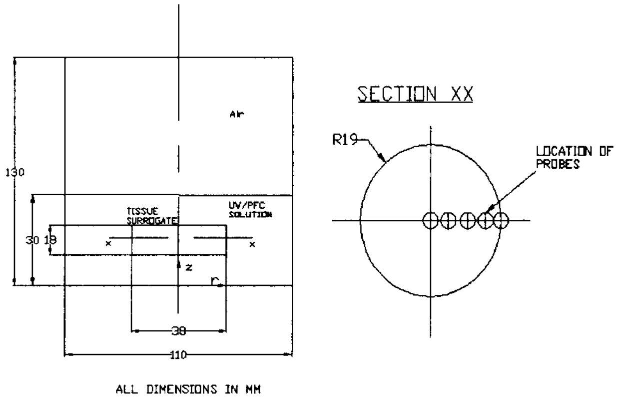

Figure 1: Experimental Setup for Simple Storage in UW/PFC solution.

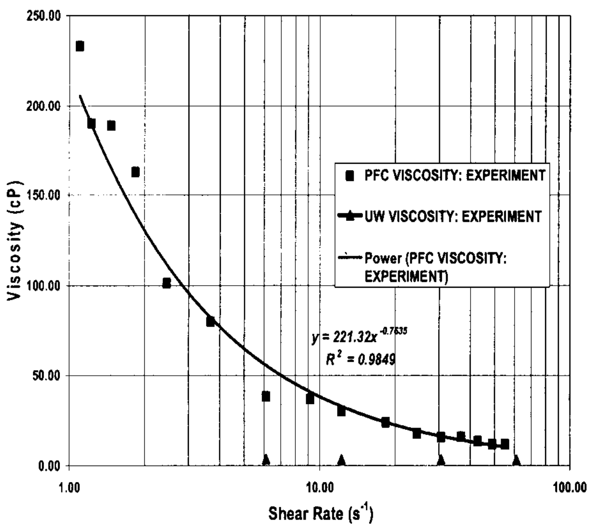

Figure 2: Viscosities of UW and PFC solutions.

The spatial temperature distribution inside the tissue surrogate during simple storage in UW and PFC solutions at various time instants from the initial state to the final steady state are as shown in Figure 3. Based on the initial conditions, the spatial temperature profile was maintained the same for both the simple storage methods at the start of the experiment. It is observed that UW solution cools the tissue faster than PFC solution with increase in time. The difference in temperature (ΔT) at each stage of the cooling process between the two methods is significant as the thermal diffusivity of UW solution is nearly four times higher than that of PFC solution. There is a 33% difference in temperature (ΔT) between the two methods from the end of 6 minutes up to 1.5 hours. This ΔT reduces gradually over time till the system reaches steady state. This has direct physiological consequence on the survival of a living tissue. Faster rate of cooling may lead to ice crystal formation and apoptotic death of cells. In contrast, slow rate of cooling may result in longer warm ischemic time; the effect of which is deleterious to the viability of a graft post transplant [Morita et. al., 1993]. In order to achieve the best functional efficacy, an optimal cooling rate has to be determined. The in-vitro experimentation of the TLM will help in analyzing the optimal cooling rate of the tissue.

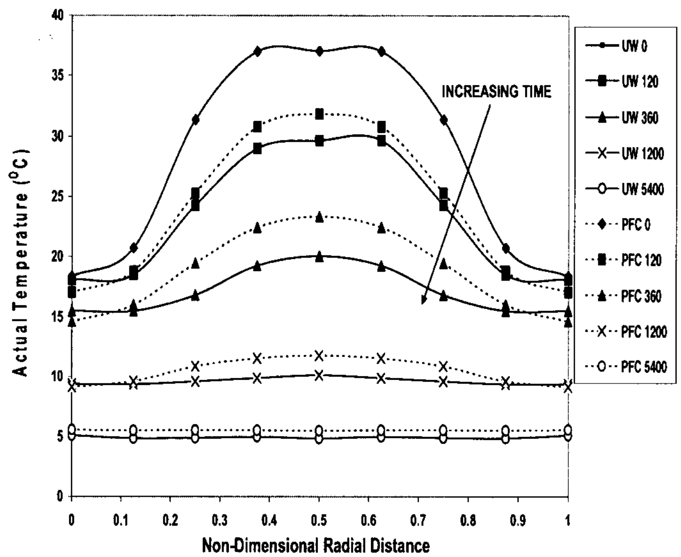

Figure 3: Spatial temperature distribution inside tissue surrogate at various time instants

CONCLUSION:

The transient temperature history and spatial temperature distribution inside pancreatic tissue surrogate during the hypothermic simple cold storage (at 4 °C) was generated using UW and PFC solutions. It is evident that the rate of cooling is significantly different in the two methods. The high magnitude of ΔT plays a very important role in the functional viability of the pancreatic tissue before islet isolation. The data generated using simple storage method also serves as a reference for the in-vitro experimentation of tissue using Two-Layer Method.

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