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TEMPERATURE AND HEAT STRESS OF VESSELS DURING COLD PERFUSION OF KIDNEY

Wang Y.B and Zhu K.*
*Author for correspondence
Tianjin Key Laboratory of Refrigeration Technology,
Tianjin University of Commerce,
Tianjin,300134,
China,
E-mail: zhukai210@tju.edu.cn

ABSTRACT

The first step of organ cryopreservation is a cryoprotectant perfusion, which can speed cooling. The temperature of the kidney decreased from 37℃ to about 0℃ by perfusion. During the kidney perfusion process, the cryoprotectant enters the kidneys through the renal artery and leaves the kidneys through the renal vein after passing through a series of capillaries. In cold perfusion vessels with a diameter larger than 0.3 mm must be treated individually. The obvious temperature change in the larger vessels will bring in the displacement causing by the thermal contraction. This paper is dedicated to present a comprehensive investigation on the thermal effects of larger blood vessels during cold perfusion including temperature change and corresponding heat stress. A structural model of heat transfer in kidney is developed using currently available anatomical and physiological data. To characterize the effect of thermally significant blood vessels on heat transfer inside the tissues during cold perfusion, the cryoprotectant in the blood vessel was controlled by the energy equation and Navier-Stokes equations. The tiny capillaries and its surrounding biological tissue were treated as the porous media following Darcy's Law. The controlling equations were numerically solved by CFD software. The numerical simulation for the coupled transient thermal field and stress field is carried out by sequentially thermal-structural coupled method based on ANSYS to evaluate the stress fields and of deformations which are established in the blood vessel and tissue. The results indicated that the thermal effects of large blood vessels could remarkably affect the temperature distribution of cold perfusion. And the heat stress obvious changed during cooling, especially for the vein. The maximal heat stress occurred at the export of the vein. This position may be the keys to avoid stress injury during perfusion. This paper provides a guideline to optimize the cold perfusion process from the biomechanics effect.

INTRODUCTION

Organ transplantation has been one of the most significant advances in medicine in the latter half of the 20th century and remains in many cases the only effective therapy for end-stage organ failure [1]. Hypothermia is employed for organ preservation to reduce the kinetics of metabolic activities. Cooling is induced by a brief flush with a chilled preservation solution after the organ is removed from the donor. Kazuhiro et al. [2] pointed out that the initial flush is equally as important as the storage itself. The improvement of this process could minimize preservation injury and supply the organ of high quality and efficacy [3,4]. Therefore, the demand for a detailed understanding of the temperature history of the organ in order to monitor the extent of cryopreservation is compelling.

During the kidney perfusion process, the cryoprotectant enters the kidneys through the renal artery and leaves the kidneys through the renal vein after passing through a series of capillaries, which will decrease the organ temperature and produce temperature gradient in biological tissue. This is a typical coupled heat transfer problems. In the bio-heat transfer calculation, the vessels with a diameter larger than 0.3 mm must be treated individually. The thermal effect of the vessels and tissue should be analyzed to provide information to clinicians for better predicting hypothermic perfusion process and making more reliable treatment decisions. In recent years, many researchers have done numerical simulation and experimental analysis on thermal stress and fracture problems in freezing preservation of organs [6-9].While the biomechanical effect during hypothermic perfusion did not attract enough attention. In the recent, kidney transplantation is one of the most common and successful organ transplantation [5]. In this paper, we focus on the initial flushing of kidney before storage.

This paper is dedicated to present a comprehensive investigation on the thermal effects on the temperature profile and thermal stress during hypothermic perfusion using a series of thermal-structure simulations. In the simulation of temperature field, the locations of large blood vessels and tissues are precisely determined; therefore, the heat and mass transfer between large blood vessels and tissues could be well simulated compared to simplified structures [10-14].

MEHOODS OF SIMULATION

Physical Model and mesh generation

The kidney is shaped much like a bean, not regular shaped. The renal vessel tree is a complex vascular net irrigating the renal tissue. The vascular cast was got by experimental method as shown in Figure 1, where the blue ones represent the vein while the red ones represent the artery. We used the 3D scanner (Shining3D, China) and Geomagic Studio 10.0 software (Geomagic, North Carolina, USA) to reconstruct the arteries, veins and tissue separately [15-17]. Taking the arteries as example, we firstly obtain the image of arteries from 3D scanner, which is then input to the Geomagic Studio 10.0 software to switch to 3D model. All parts of the reconstructed subjects were saved as IGES format for importing into pro/E4.0.The 3D geometric model of porcine kidney comprises tissue, large arterial and venous vessels are shown in Figure 2. After Boolean operation and assembly, the model was switched to ICEM CFD 13.0(ANSYS, Inc., Canonsburg, PA, USA) for computational meshing. Unstructured tetrahedral meshing scheme was used. We first generate mesh for artery and vein and then we generate mesh for tissue domains to ensure high quality of mesh in each component and at the interface between different tissues. The surface mesh from the fluid domain was used in the solid domain to enable a better interpolation of fluid– solid interfaces. The number of total tetrahedral elements is 2,692,000. For arteries, veins and tissue domain, the number of elements for each component of kidney are 1,009,367; 455,782 and 1,226,851.

Figure 1 Renal vascular cast

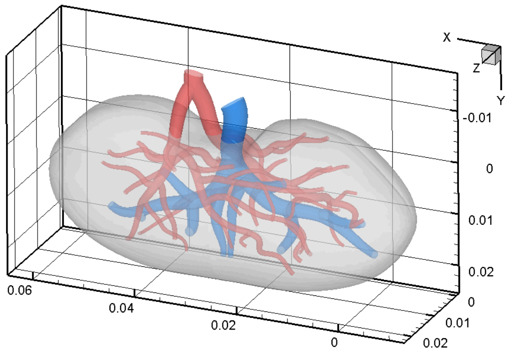


Figure 2 The physical model established by Proe

After creating mesh for each component, the governing equations together with boundary conditions are solved using Ansys CFX 13.0(ANSYS, Inc., Canonsburg, PA, USA),which is a commercially available finite element software package and extensively utilized to address avariety of practical engineering problems nowadays. The flow and temperature analysis are solved according to SIMPLE and second order upwind algorithms. The first order implicit time discretization scheme is used for time evolution. All simulations adopted parallel model and run on the DAWNING workstation with 30 core CPUs and eight memories (1 GB each).

Description of hypothermic perfusion experiment

The kidney was removed from the abdomen and flushed at ambient room temperature with the solution pre cooled to +1℃. During the hypothermic perfusion, the average perfusion rate was 0.8ml/min (0.05m/s). The coolant fluid enters the kidneys through the renal artery and leaves the kidneys through the renal vein. We focus on the temperature change during the hypothermic perfusion process, so the physiological saline rather than expensive organ preservation solution was used in the experiment.

Fluid domain model

The metabolic heat production is not considered in the simulation, for cooling could reduce the metabolic activities. The medium is continuous, and the governing equations consist of continuity, momentum and energy conservation equations.

Continuity equation:

$$\frac{\partial}{\partial x_i}(\rho u_i) = 0 \tag{1}$$

Momentum equation:

$$\frac{\partial}{\partial t}(\rho u_i) + \frac{\partial}{\partial x_j}(\rho u_j u_i) = -\frac{\partial P}{\partial x_i} + \frac{\partial}{\partial x_j}\left(\mu\left(\frac{\partial u_i}{\partial x_j}\right)\right) \tag{2}$$

Energy equation:

$$\frac{\partial}{\partial t}(\rho T) + \frac{\partial}{\partial x_i}(\rho u_i T) = \frac{\partial}{\partial x_i}\left(\frac{k}{c_p}\left(\frac{\partial T}{\partial x_i}\right)\right) \tag{3}$$

In the present study, the boundary condition is set up according to the hypothermic perfusion experiment. The uniform velocity profile is adopted at the entrance of artery. The coolant is physiological saline whose temperature is 1℃ and velocity is 0.5m/s. The maximum Reynolds numbers of perfusion model, based on the inlet diameter which is 245 and thus the flow was treated as laminar. The outlet of artery and the inlet of vein were set as interface in the CFX. In the simulation, the initial temperature of the biological tissue and blood is 310 K. On the whole, the physiological saline properties were almost identical to that of water which assumed as incompressible and Newtonian flow with a constant density of 1000 kg/m^3 and a constant dynamic viscosity of 1.7921×10^{-3}Pa· s.

Porous model

Tissues can be treated as a porous medium[19, 20] as it is composed of dispersed cells separated by connective voids which allow for flow of nutrients, minerals, etc. to reach all cells within the tissue. Taking the tissue as porous media could establish the continuous transport channel in the kidney in the simulation. The porous media approach involves the application of the principle of heat transfer and fluid mechanics in a fluid-saturated perfused tissue to obtain a model of equation that will govern heat transfer and fluid flow in a biological system (living tissue). It is assumed that the tissue is isotropic. The porosity (volume fraction of the vascular space) is 0.2 [21,22] and the thermal conductivity is$0.5\mathrm{W/(m\cdot k)}$[23].

As the isolated kidney was exposed in the air during coolant perfusion, the boundary condition for kidney surface adopts the convective boundary condition.

$$-k\frac{\partial T_s}{\partial n} = h_a(T_s - T_a) \quad (4)$$

where, Ts is the renal surface temperature, $\mathrm{h_a} = 10\mathrm{W/(m^2\cdot K)}$ and $\mathrm{T_a} = 26$ ℃ aretheconvectiveheattransfercoefficientand temperature of air in ambient.

Coupled thermomechanical analysis

Workbench provides the capability of performing indirect sequentially coupled thermo-mechanical analysis for both heat and stress analysis. In this study, the thermal and structural analyses were performed using Ansys CFX and ANSYS Mechanical through Workbench (ANSYS, Inc., Canonsburg, PA, USA). A transient thermal analysis was performed first to obtain the global temperature history generated during the cold perfusion. A transient stress analysis is then developed with an automatic exchange of the element type from thermal-to-structural, and applying the temperatures obtained from previous transient thermal analysis, as a thermal loading for the mechanical analysis[24,25]. The modulus of elasticity, Poisson's ratio and coefficient of thermal expansion respectively were obtained by experiments [26,27] as shown in Table 1.

Table 1 Mechanical parameters of kidney

Modulus of elasticity	Poisson's ratio	Thermal expansion coefficient
0.43 (MPa)	0.33	2.46×10^{-5}(1/℃)

RESULT AND DISCUSSION

The cold perfusion by introducing chilled solutions in sufficient volumes (clinically this requires in the region of 200-400ml of chilled solutions) into the major vascular channels can wash out the blood and achieve moderate cooling. The temperature variation and consequent thermal stress and deformation are the result of hypothermic perfusion. The coupled calculations provided a complete set of data including temperature and mechanical data including displacement and intramural stress distributions on the tissue during the whole hypothermic perfusion process.

Temperature field of kidney

The CFD simulation focuses on the three domains: arteries, tissue, and veins, which are modelled as a conjugate heat transfer problem. During the kidney perfusion process, coolant fluid enters the kidneys through the renal artery and leaves the kidneys through the renal vein after passing through a series of capillaries. Figure 3 is the streamline of the coolant fluid which shows this flowing process. Heat and mass transfer constantly take place in the inner and outer of kidney.

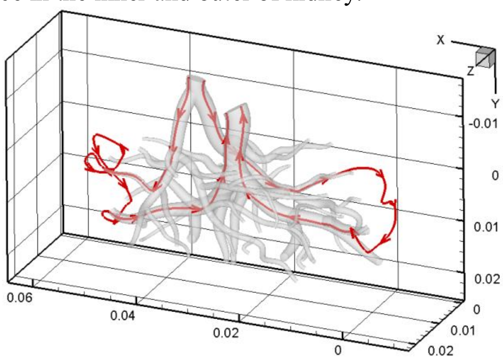
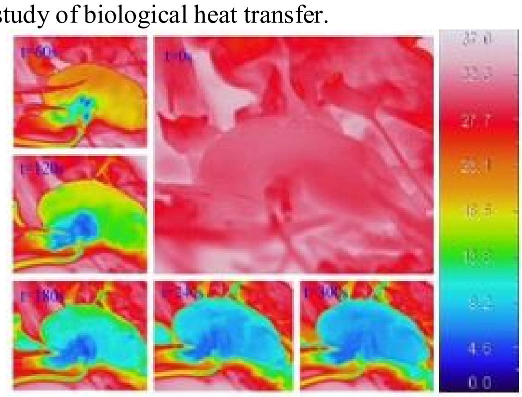
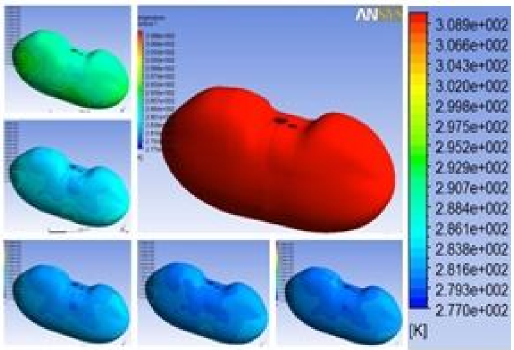


Figure 3 The streamline of coolant in the kidney

As mentioned above, a hypothermic perfusion experiment was conducted by the clinician. The hypothermic perfusion lasted 300 seconds and the infrared images of kidney were taken as shown in Figure 4A. Figure 4B shows the variation in the temperature versus time during the total time simulation of perfusion process for a kidney. The lowest temperatures occur near the renal arterial of the kidney. The temperature continued to decline and a larger temperature gradient occurred around the arterial entrance of the kidney due to continuous filling of coolant. The irregular configuration of renal vessels leads to an uneven temperature distribution on the kidney surface. We can conclude that the configuration of vessels is an essential factor in the study of biological heat transfer.



A Infrared images taken in the hypothermic perfusion experiment



B Temperature distribution of simulation result

Figure 4 Surface temperature field obtained from numerical simulation and infrared image

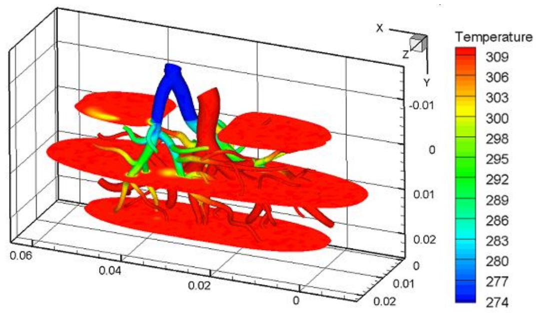
Table 2 gives the temperature range of surface temperature at different times. The temperature difference between the maximum and minimum value is about 17.6℃ at the moment of t=20s, and then, it decreases with time. That is to say, the temperature gradient is larger at the beginning and the kidney achieves uniform temperature of ~4℃ at the end of perfusion. The comparison between the simulation results and the infrared thermal images shows that the trend of the temperature field on kidney surface is roughly the same during the cooling process, which could ensure the accuracy of subsequent calculations.

Table 2 Temperature range at different time during cooling

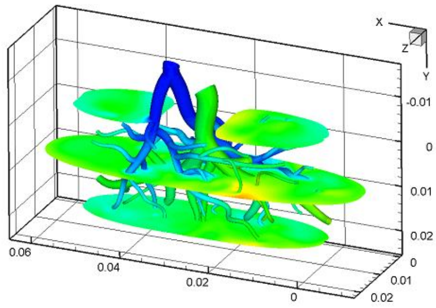
	20s	30s	60s	120s	180s	240s	300s
Temp. range(℃)	30.8~ 13.2	27.0~ 11.8	18.6~ 8.7	10.3~ 5.7	7.4~ 4.6	6.3~ 4.2	5.9~ 4.1
Temp. Different(℃)	17.6	15.2	9.9	4.6	2.8	2.1	1.8

Temperature of renal vessels

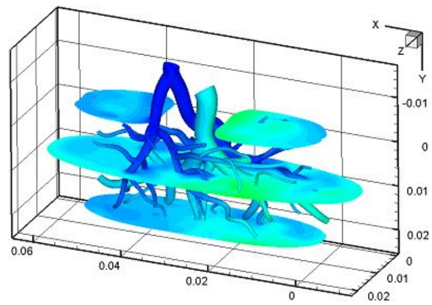
The fluid flow heterogeneity in the kidney is largely determined by anatomical features of the vascular tree[10].The complex tree structure with irregular dichotomous tree has been more accurately described by the 3D scanner. The cooled fluid enters the kidney through the renal artery and flow along the vessels. Structure induced fluid-flow heterogeneity significantly limited the heat transfer property of the vessel. Figure 5 shows the temperature field of vessels during hypothermic perfusion. At the beginning of the flushing, the temperature gradient of artery is larger. The fluid temperature raises from +1℃ to ~37℃ when leaves the artery as shown in Figure 5A. Thus, the veins still keep the initial temperature at the beginning of the perfusion. After a period of time, the fluid whose temperature is less than 37℃ after passing through a series capillaries enters the renal veins as shown in Figure 5B. The veins' temperature begins to decrease. The more uniform temperature appeared in the veins at every moment for the smaller temperature differences between the fluid and tissue. The average temperature of veins is higher than that of arteries. After 150s, the artery temperature keeps constant shown in Figure 5E. However, the vein artery decreases to about 4℃ after perfusion for 200s. The whole temperature including the fluid, the tissue achieved the uniform temperature after 300s.



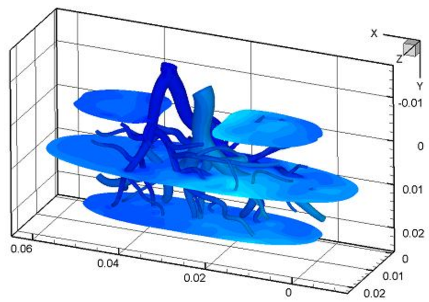
A 10s



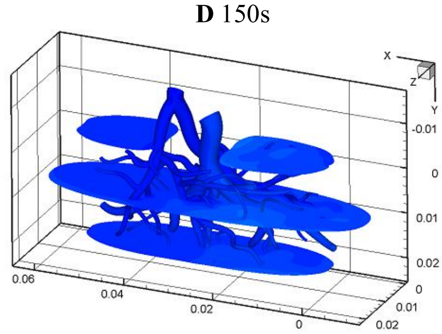
B 50s



C 100s



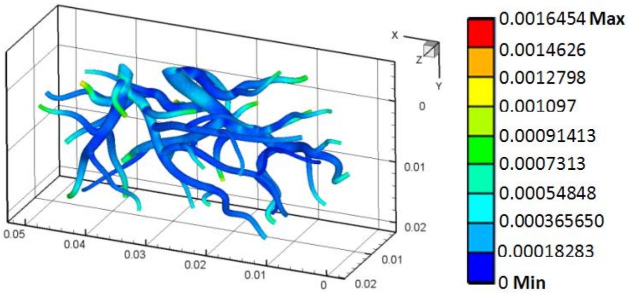
D 150s



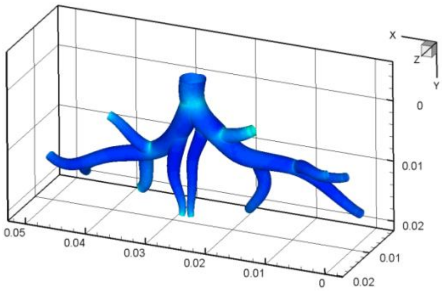
E 200s

Figure 5 Heat temperature of blood vessels

Figure 6 presents the distribution of the constraint equivalent of Von Mises stress at 50s, and the scale of values varies from 0KPa to 1.6KPa. The relatively higher Von Mises stress appears at the terminus and bifurcation point, for the larger temperature gradient in these locations. The branches made the fluid flow decrease and thus the decreased cooling capacity and higher temperature gradient. As can be seen from Figure 5, vessel diameter decreases to a small value after successive generation of branches. The smaller diameter enhanced the heat transfer capacity and lead to larger Von Mises stress. That is to say, the stress injury is likely to occur in small vessels. Figure 6B shows that the Von Mises stress of veins is relatively smaller. However, the artery wall is more rigid and thicker. Thus, the larger diameters of veins can prevent it from being damaged by stress.



A Von Mises stress of arteries



B Von Mises stress of veins

Figure 6 Von Mises stress of blood vessels

The average temperature and Von Mises stress are shown is Table 3. Both temperature and Von Mises stress change significantly at the first 200s. After 200s, there are no obvious variation in temperature and thermal stress. We should pay special attention on the biotissue for the prior to 200s at flushing.

Table 3 The values of average temperature, cooling rate, thermal stress of the arteries and venous of porcine kidney on different time

	artery		vein	
Time/s	Temperature /K	Stress/Pa	Temperature /K	Stress/ Pa
10	305.828	1645.3	308.021	274.4
20	301.650	2193.8	303.741	1305.5
30	297.761	2332.1	299.455	2100.8
40	294.527	2775.2	295.952	2449.1
60	289.536	3843.3	290.547	2630.6
180	278.997	6135.4	279.957	3015.8
300	277.676	6423.3	277.731	3064.0

The coupling result of internal kidney

The longitudinal section were chosen as research object and shown in Figure 7. Large blood vessels embedded into the kidney through the contribution to heat transfer by cryoprotectant flow could lead to the significant temperature nonuniformity around the vessel and steepy temperature gradient as shown in Figure 8A. Thus, the perivascular tissue produces greater Von Mises stress as shown in Figure 8B. It was found that the Von Mises stress decreased gradually along the radial direction of vessels. The tissue away from the vessels produce less thermal stress due to the seepage flow effect of porous media leading to more uniform temperature distribution. The inner distortion deformations are more dependent on the vessel structure. The very outer edge of the kidney shows the maximum thermal strain, especially for the left and right edge of the kidney in the Figure 8C. The cooling causes the contraction of the tissue. The displacement of internal tissue constrained by the traction of surrounding tissue, while tensile stress imposed on the outer tissue all come from internal of kidney. The thermal deformation of external surface is the comprehensive reflection of internal deformation of kidney during perfusion. Each of the kidneys is about 10cm long and 5.5cm wide. So the maximum deformation occurred in the longitudinal direction. The left and right tip of the kidney should deform seriously.

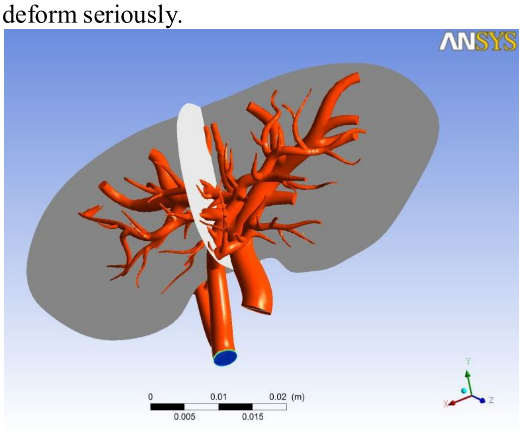
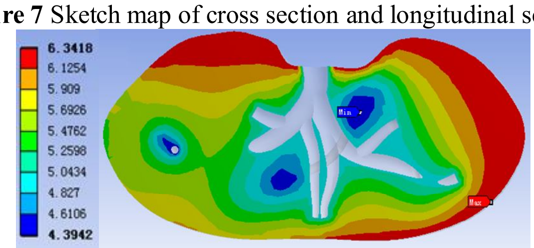
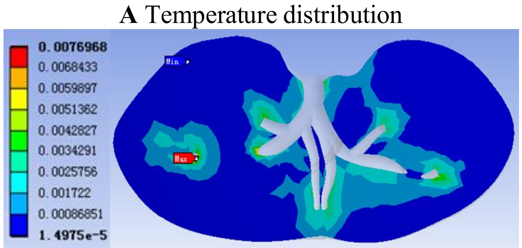


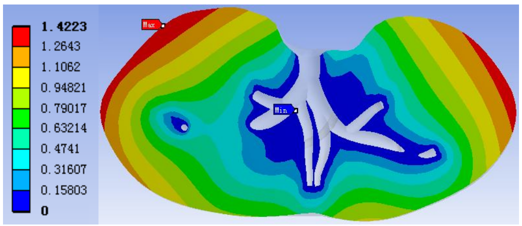
Figure 7 Sketch map of cross section and longitudinal section



A Temperature distribution



B Von Mises stress distribution



C Distortion distribution

Figure 9 The coupling result of longitudinal section when perfusing for 240s

Jacobsen et al.[3] reported that a highly deleterious effect on post-transplant function of rapid cooling of rabbit kidney before storage. They attributed this to patchy necrosis of proximal tubular cells as well as considerable amounts of cellular debris in tubular lumina. The proximal tubular occupies the cortical labyrinth, where the larger deformation takes place according to thermal structure simulation. We concluded that the rapid cooling during washout of kidney grafts before cold storage is undesirable as such cooling produces a larger magnitude of displacement and consequent nonfunctioning transplants. Van Wagensveld et al.[28] pointed out that flushing at 37 ℃ following cold storage could attenuates the reperfusion injury in preserved rat livers. Flushing at 37 ℃ could avoid the generation of temperature gradient. Thus, this is another evidence to illustrate that kidney injury occurs due to the temperature gradient and consequent deformation. In another view, using lower flow velocity during the initial flush may lead to irregular distribution of the solution and incomplete flushing of blood components from vascular beds[29]. Thus, there exists an optimal perfusion rate. The coupling calculation of the temperature field and thermal stress distribution provide a platform to optimize the perfusion protocol by simulation method.

CONCLUSION

This paper presents a comprehensive investigation on 3-D tissue temperature profile of kidney during hypothermia perfusion and consequent thermal stress and deformation based on a thermal structure coupling calculation for an anatomical model of kidney. In the simulation of temperature field, the large blood vessels were reconstructed according to anatomical structure and the micro-capillaries and tissue were treated as the porous media so as to form the continuous channel of the vessel in the kidney. The comparisons between calculation result and infrared images taken during cold perfusion illustrate that this kind of calculation can give a true reflection of temperature.

The numerical simulation for the coupled transient thermal field and stress field is carried out by sequentially thermal-structural coupled method based on ANSYS Workbench to evaluate the stress fields and deformations which are established in the kidney during hypothermia perfusion. The simulation results shows that the thermal effects of large blood vessels remarkably affect the temperature, thermal stress and deformation distribution of kidney. The maximum thermal stress occurs near the vessel and the largest deformation takes place around the tips of the tissue surface. Additionally, increasing the perfusion could significantly affect the magnitude of the thermal effects of large blood vessels. The larger thermal stress occurs at the terminals and the bifurcation points. It is worth to further analyze the thermal effect on the kidney injury during hypothermia perfusion and optimize the perfusion protocol.

ACKNOWLEDGEMENTS

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