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CONJUGATE COOLING PROTOCOLS FOR HUMAN HEARTS INCLUDING EPICARDIAL BLOOD VESSELS

Abas Abdoli[1], S.M. Javad Zeidi[2], and George S. Dulikravich[2]
[1] Rocky Research, 1598 Foothill Drive, Boulder City, NV 89005, USA, ab.abdoli@gmail.com
[2] MAIDROC Laboratory, Department of Mechanical and Materials Eng., Florida International University, 10555 W. Flagler St. Miami, FL 33174, USA {szeid001, dulikrav}@fiu.edu

SUMMARY

Computational analysis of forced conjugate convection cooling of realistic human hearts including main epicardial blood vessels was performed. It was found that including the main epicardaial blood vessels in the forced conjugate cooling analysis accelerated the cooling process and reduced temperature irregularities in the heart tissue, suggesting that usable life of transplantation bound human hearts can be extended from 10.2 to 11.5 hours after extraction from the donor’s body.

Key words: *cooling protocols, cryopreservation, rewarming, thermal stresses, optimized cooling*

1 INTRODUCTION

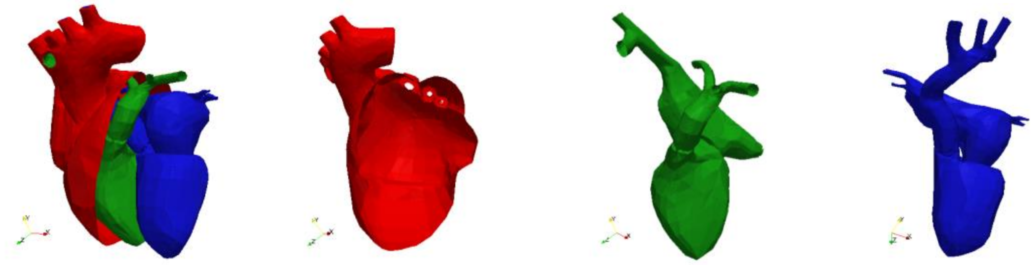
An empirical relationship based on experimental evidence, known as ‘‘Q_{10} law’’, states that for every 10°C reduction in tissue temperature, there is a corresponding reduction in cell metabolic rate equal to the constant Q_{10}. The law is written as:

$$\frac{q_m}{q_{m0}} = (Q_{10})^{\left[(T-T_0)/10\right]} \tag{1}$$

Here, T is the living tissue temperature in degrees Celsius and q_m is the cell metabolic rate. Values for Q_{10} range from 2.0 to 3.0 and are cited in the physiology literature [1]. For example, assuming the worst situation where Q_{10} = 2.0, it can be observed that reducing temperature from +37°C to +27°C reduces the metabolic rate by 50%. Reducing temperature to +4°C would reduce the metabolic rate in the same scenario by 89.9%, thus significantly reducing oxygen and glucose consumption and carbon dioxide production. The conclusion is that the cooling of 3D organs should not only be done quickly, but also as uniformly as possible. Temperature uniformity must be accomplished in order to minimize the amount of time when parts of the organ are still at an elevated temperature, thus experiencing high local metabolic rates. Our early efforts in simulating cooling of a canine kidney and a human brain accounted only for heat conduction [2, 3]. Our recent computations simulating optimized conjugate cooling protocols of a fully 3D realistic human heart without accounting for the main epicardial blood vessels [4, 5] suggest that the usable life of an extracted heart can be extended from the current 4.5 hours (using non-circulating cold saline bath) to 10.2 hours. This paper extends this recent study and suggests that the usable life of a heart can be further extended to 11.5 hours by perfusing also the main epicardial blood vessels, thus, enabling transport of hearts across the entire north American continent.

2 METHODOLOGY

The human heart geometry used for simulations was obtained from 3D, high resolution CT scans. Figure 1 demonstrates different domain surfaces of the heart in different colors. The blood contact surfaces consisting of the right (pulmonic) and left (systemic) heart circulations domains are shown in green (Fig. 1a & 1c) and blue (Fig. 1a & 1d), respectively. Figures 1a & 1b show the outermost surfaces in red.



a) b) c) d)

Figure 1. Heart surfaces: a) all surfaces, b) outermost surfaces, c) heart pulmonary circulation domain surfaces, and d) heart systemic circulation domain surfaces.

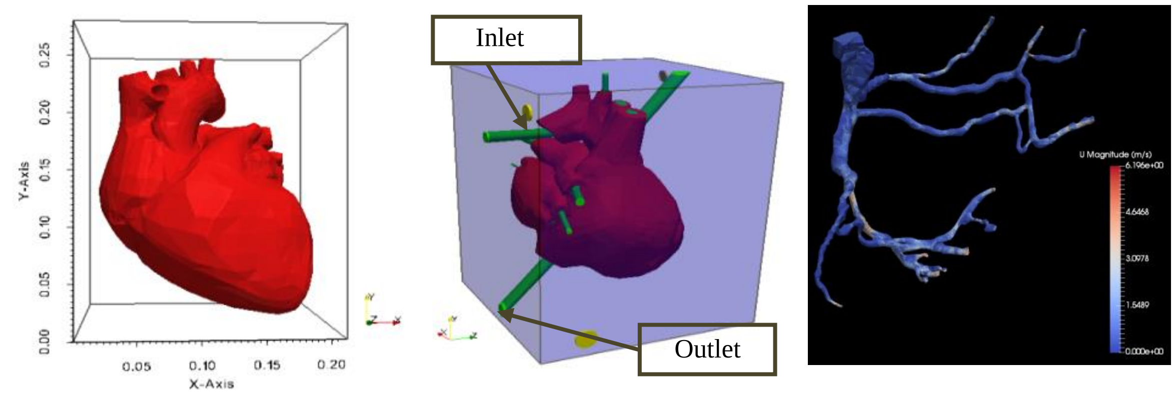


Figure 2. Cooling container with the heart (left), cooling container with inlets and outlets indicated (middle), and an epicardial blood vessel imbedded in the heart tissue.

A hexahedra (Figure 2) of 214 mm in length, 212 mm in width and 282 mm in height was virtually created as the heart-cooling container. For circulating the coolant outside of the heart, two inlets with 15 mm diameter and two outlets with 20 mm diameter were designed on the cooling container walls. These inlets and outlets were designed to create cooling fluid jets and vortices around the heart, thus, enhancing convection heat transfer. For internal cooling, two inlets and two outlets were designed for each of the heart right and left circulation loops. University of Wisconsin (UW) solution was used in simulations as the cooling liquid with constant inlet temperature of +4°C. Outlet pressure of the epicardial blood vessel was enforced to be atmospheric, while average inlet coolant speeds were 1 m/s (external circulation loop), 0.4 m/s (heart pulmonary circulation), and 1.0 m/s (heart systemic circulation). All cooling container walls were assumed to be thermally insulated in all cooling scenarios. Fully 3D unsteady conjugate conduction/convection heat transfer analyses were performed by solving the fully 3D governing equations for fluid and solid domains. For turbulent coolant flow cases, $k-\varepsilon$ turbulent model equations were added to Navier-Stokes equations for the external flow domain. 3D stress analyses were also performed to calculate thermal and hydraulic stresses during the cooling process. All numerical simulations were performed using OpenFOAM software platform on a 16 processor parallel computer [4, 5].

3 RESULTS AND CONCLUSIONS

A number of conjugate cooling protocol cases were simulated using various boundary conditions. The most successful was Case 5 which involved forced convection cooling of inside surface of the heart and simultaneously forced convection cooling of the outside surface of the heart. Figure 3 shows results of cooling in Case 5 depicted at 300 seconds. Figure 3a illustrates the UW solution streamlines around the heart with velocity distribution. This figure displays that the maximum velocity of coolant occurred at the inlets. In comparison, the minimum velocity occurred at fluid-solid interfaces due to fluid viscosity. The heart model and its connections were added to this figure to better demonstrate the UW solution streamlines pattern around the heart. Thus, its red color is not an indication of the velocity or temperature. Figure 3b shows the temperature distribution of the UW solution around the heart at 300 s showing the maximum temperature (+5.79°C) occurring at the place where the fluid was in direct contact with the surface of the heart. The cut-away views of the heart shown in Figure 3c reveal one large hot spot located above the right ventricle, and on the right side of the right atrium. Two more hot spots can be observed in Figure 3d: one is located on the left side of the left ventricle and the other is located on the right side of the left atrium. Thus, these three hot spots will take longer to cool compared to the rest of the heart tissue due to ticker heart walls in these regions. Case 5 results of cooling are shown in Fig. 4 for 3600 s of cooling. It is immediately apparent that combined conduction and convection (moving coolant inside and outside the heart) results in considerably faster and more uniform cooling of the entire heart.

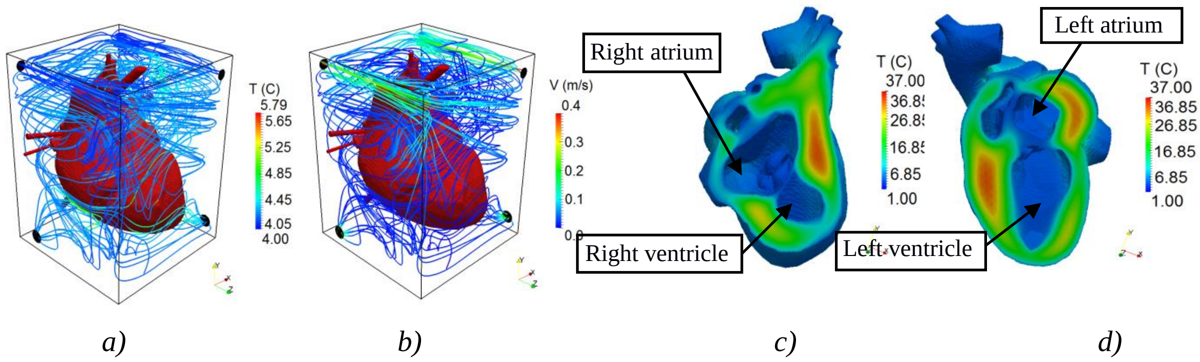


Figure 3. Results at 300 seconds: a) temperature distribution of external flow streamlines, b) speed distribution, c) temperature distribution inside the heart (1st cut-away view), and d) 2nd cut-away).

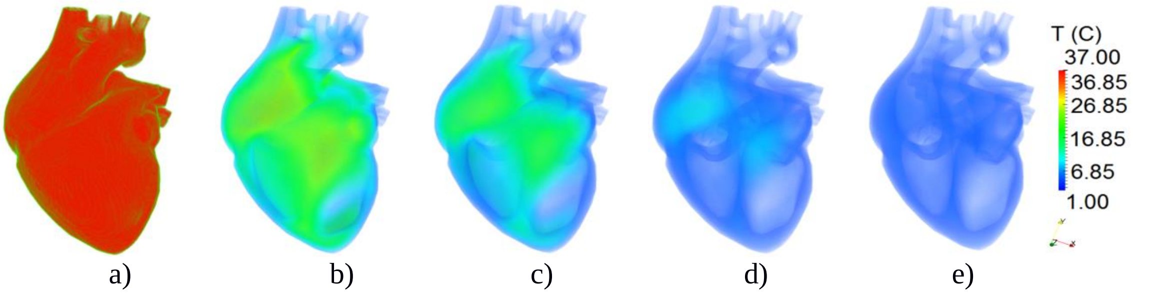


Fig. 4. Temperature distribution of the heart at: a) 0 s, b) 300 s, c) 600 s, d) 1500 s, and e) 3600s

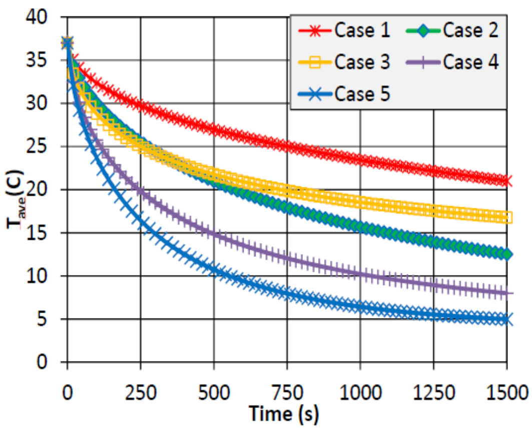


Figure 5. Average temperature variation with time in the heart tissue for the five test cases [5].

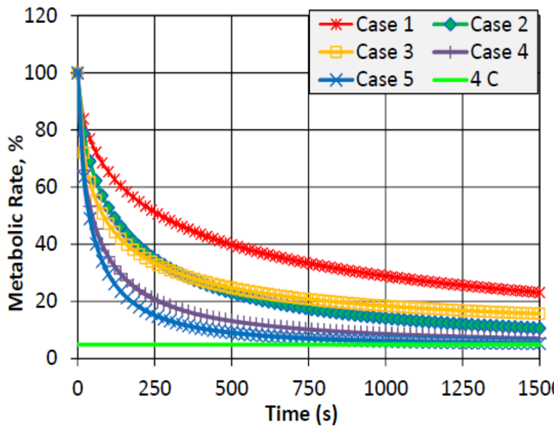


Figure 6. Average metabolic rate variation with time in the heart tissue for the five test cases.

These two figures show that simultaneous forced convection cooling of inside and outside surfaces of the heart is the most promising general approach to uniformly cooling the heart [4, 5].

In the next step, the stress analyses were performed by using the data obtained by the thermo-fluid analysis results. Normal and shear forces applied by the coolant flowing along the innermost and outermost surfaces were used as the boundary condition of these surfaces. These values were updated for each time step. The heart temperature field was used to obtain the thermal stresses during the cooling process. The ultimate tensile stress of the heart tissue was assumed to be 110 kPa. The maximum value of calculated von Mises stress was 103.67 kPa at 1800 s. This shows that the effect of thermal stresses was not significant due to the very small Young's elastic modulus and thermal expansion coefficient of the heart tissue. The importance of these simulations was to show that maximum pressures within the pulmonary and systemic circulatory domains remained less than 110 kPa (~ 80 mmHg).

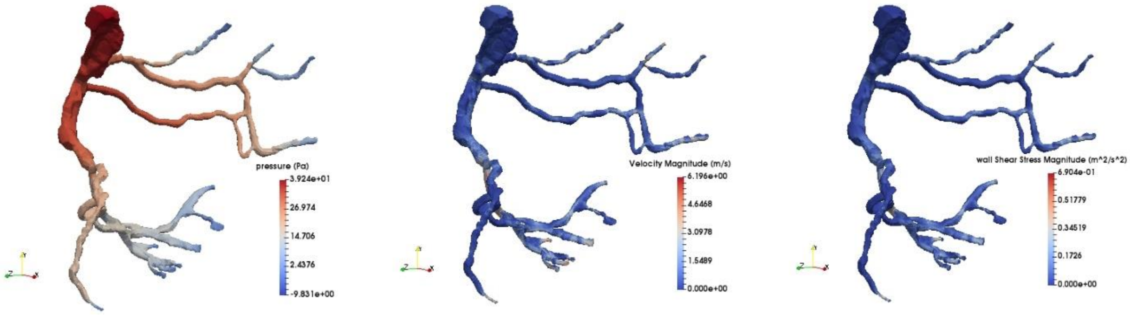


Figure 7. Predicted distributions of pressure (left), local average speed (middle), and wall shear stress (right) in an epicardial blood vessel perfused by UW solution with inlet speed of 0.5 m/s.

The fully conjugated forced convection cooling protocol (Case 5 in Figures 3-6) reduced the average temperature of the heart to +5°C after 1500 s, which was 70% lower temperature than currently achievable by purely conduction/natural convection cooling in a stagnant saline solution. The resulting stress analyses of the conjugate forced cooling indicated that von Mises stresses were lower than the maximum allowable tensile stress of the heart tissue. Details of these results were published [4, 5], suggesting that by using simultaneously internal and external forced convection it is possible to preserve a human heart for 10.2 hours.

When incorporating three main epicardia blood vessels (coronary arteries and cardiac veins such as shown in Figure 7) in the internal forced convection cooling loop, the heart was cooled even faster and more uniformly. Consequently, using the same value of Q10 coefficient from equation (1), this more detailed heart geometry allowed for extending the extra-corporal life of the extracted heart to 11.5 hours. This time will comfortably cover the time required to locate the donor and harvest the heart (1.0 hours), extraction site-to-airport transportation time (1.0 hour), receiving airport-to-transplantation site transportation time (1.0 hour), and implantation time (1.0 hours). This will leave 7.5 hours for air transportation which is sufficient to cover the entire inhabited part of the North American continent and the Caribbean.

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