Computer Simulation of Blood Flow, Left Ventricular Wall Motion and Their Interrelationship by Fluid-Structure Interaction Finite Element Method*

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To simulate fluid-structure interaction involved in the contraction of a human left ventricle, a 3D finite element based simulation program incorporating the propagation of excitation and excitation-contraction coupling mechanisms was developed. An ALE finite element method with automatic mesh updating was formulated for large domain changes, and a strong coupling strategy was taken. Under the assumption that the inertias of both fluid and structure are negligible and fluid-structure interaction is restricted to the pressure on the interface, the fluid dynamics part was eliminated from the FSI program, and a static structural FEM code corresponding to the cardiac muscles was also developed. The simulations of the contraction of the left ventricle in normal excitation and arrhythmia demonstrated the capability of the proposed method. Also, the results obtained by the two methods are compared. These simulators can be powerful tools in the clinical practice of heart disease.

Key Words: Biomechanics, Computational Mechanics, Finite Element Method, Fluid-Structure Interaction Analysis, Electro-Physiology

1. Introduction

The heart, especially the left ventricle (LV), plays a central role in the circulation of blood; thus, it is one of the essential organs for supporting human life. Although recent advancement in cellular and molecular technologies has clarified the fine structure and function of the heart at the microscopic level⁽¹⁾, these approaches have contributed little to the understanding of the integrated function of this organ as a pump. If these fine pieces of information are put together, it will surely promote our understanding of the heart in the healthy and diseased states; however, the complex nature of the system certainly requires the power of computational science.

Each contraction of LV proceeds in the following sequences⁽²⁾: Phase 1 (isovolumic contraction period, about 0.1 sec duration) begins when wall tension starts to develop by the contraction of the ventricular myocardium. The resultant increase in left ventricular pressure (LVP) first closes the mitral valve. Then, LVP continues to rise until it exceeds the aortic pressure (AP) (about 9 300 Pa (70 mmHg)), which causes the aortic valve to open. Phase 2 (ejection period, about 0.2 sec duration) begins when the aortic valve opens and blood is ejected into the aorta. During the ejection period, AP first rises to the peak of about 16 000 Pa (120 mmHg) because blood is ejected into the aorta faster than it flows out from the aorta to peripheral circulation, then LVP falls gradually as the ejection becomes slow. At the end of ejection, the ventricular volume (end-systolic volume: ESV) is about 40 to 45 percent of the volume at the beginning of ejection (end-dias-

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tolic volume: EDV, about 120 ml in adult human); thus, about 55 to 60% of the blood volume is ejected (ejection fraction). Phase 3 (isovolumic relaxation period, about 0.1 sec duration) begins after aortic valve closure, and the body circulation (afterload) is disconnected from the LV. As both the aortic and mitral valves are closed, relaxation of the myocardium proceeds isovolumically. Relaxation continues until LVP falls below the left atrial pressure (LAP) to open the mitral valve again. Mitral valve opening initiates phase 4 (filling period, about 0.6 sec duration), during which blood flows across the mitral valve from the left atrium into the relaxed LV. During this phase, as the LV is filled, LVP rises gradually for the next contraction (ventricular preload).

To construct a comprehensive model of the heart which accurately simulates the series of events described above, microscopic as well as macroscopic mechanisms should be incorporated. Models of the electrical activity of cardiac cells have been proposed⁽³⁾⁻⁽⁷⁾ and based on these models, Winslow et al.⁽⁸⁾ and Nakazawa et al.^{(9),(10)} performed electrophysiological computer simulations of arrhythmia. In the field of excitation-contraction coupling, four-state models^{(11),(12)} are widely used. Sunagawa and Sagawa simulated the function of a combined ventricular-aortic system based on the time-varying elastance model⁽¹³⁾. At the macroscopic level, the motion of LV muscle was simulated by Tokuda and co-workers⁽¹⁴⁾⁻⁽¹⁸⁾ and Feng et al.⁽¹⁹⁾ Blood flow was simulated by Iwase et al.⁽²⁰⁾, and recently, Lemmon et al.⁽²¹⁾ and McQueen et al.⁽²²⁾⁻⁽²⁴⁾ performed the fluid-structure interaction analysis using immersed boundary methods. However, so far, none of these models can adequately simulate blood flow and wall motion of the heart based on microscopic knowledge.

The objective of this study is to develop a fluid-structure interaction (FSI) finite element based simulation program incorporating the propagation of excitation and contraction mechanisms of cardiac muscles to simulate the pumping action of human LV. An arbitrary Lagrangian Eulerian (ALE) finite element method with automatic mesh updating is formulated for large domain changes, and a strong coupling strategy is taken. Some simplifications are made for the excitation and propagation models, i.e., the FitzHugh-Nagumo (FHN)^{(4),(5)} model is employed, and the four-state model proposed by Peterson et al.⁽¹¹⁾ is employed for excitation-contraction coupling. A constitutive equation for cardiac muscles proposed by Lin and Yin⁽²⁵⁾ is employed. We also developed a static structural FEM code by eliminating the fluid dynamics part from the FSI code under the assumption that the inertias of both fluid and structure are negligible and

fluid-structure interaction is restricted to the pressure on the interface. The difference in results obtained by these two methods is shown. Finally, simulations of LV contraction in normal electrical activation and arrhythmia are presented, and the versatility of the proposed methods is investigated. It is demonstrated that the present simulators can be useful tools for clinical diagnosis and serve as a therapeutic guide in the practice of heart disease care.

2. Electrophysiological and Muscle Contraction Models

2.1 Excitation and propagation model

Myocardial cells are excited and contract when electrical stimulations are imposed. Membrane potential, which is the intracellular potential taking the extracellular potential as ground state, is between -80 mV and -90 mV at the end of diastole. When myocardial cells are stimulated, the membrane potential starts rising and if it exceeds the threshold, (approximately -60 mV), intracellular potential further rises rapidly to generate an action potential. This phenomenon is called excitation⁽²⁾.

In this paper, the FHN model^{(4),(5)}, the simplest model of membrane action potential, is employed. All the myocardial cells are electrically connected by a gap junction located in the intercalated disc, and the action potential that initiates in the sinoatrial node propagates to all the myocardial cells. The FHN model together with the monodomain propagation model is given by^{(3)-(5),(9)}

$$\dot{x}_i = c \left(y_i + x_i - \frac{x_i^3}{3} \right) + z_i + g \sum_j (x_j - x_i), \quad (1)$$

$$\dot{y}_i = \frac{-(x_i - a + by_i)}{c}, \quad (2)$$

where x and y are the variables which represent to the membrane potential and the adiphoria, respectively, z is the external stimulation, g is the conductance, and a , b , and c are the constants. The suffix i denotes the spatial position of a unit (a finite element in this paper), and j indicates the units surrounding the unit i .

2.2 Excitation-contraction (E-C) coupling

After the excitation, the following sequences of subcellular events lead to the contraction of myocardial cells⁽²⁾:

- 1) depolarization of membrane potential (action potential),
- 2) influx of Ca^{2+} ion through the ion channel, which in turn triggers the release of Ca^{2+} ion from the intracellular store site (sarcoplasmic reticulum: SR),
- 3) binding of Ca^{2+} ion to troponin C (TnC) on the thin filament reverses the inhibition to allow the interaction between actin molecules on the thin filaments and myosin molecules on the thick filaments,
- 4) myosin and actin bind to make a cross-

bridge to generate active force, and 5) muscle contracts by the sliding action of the thin and thick filaments. In this paper, the following four-state model presented by Peterson et al.⁽¹¹⁾ is employed to describe these events.

To combine the FHN model for membrane depolarization and the four-state model for E-C coupling, the phasic change in Ca^{2+} ion concentration triggered by the depolarization of the membrane potential was assumed by the following function⁽¹¹⁾:

$$[\text{Ca}^{2+}]_f(t) = [\text{Ca}^{2+}]_{\max}(t/\tau_{\text{Ca}})\exp(-t/\tau_{\text{Ca}}), \quad (3)$$

where $[\text{Ca}^{2+}]_{\max} = 1.2 \mu\text{M}$ and $\tau_{\text{Ca}} = 80 \text{ m sec}$ ⁽¹¹⁾. Although, Ca^{2+} ion concentration depends on the duration of the plateau in the action potential in reality, the duration in the FHN model is an arbitrarily given constant. Therefore, the FHN model is used as a trigger to determine the time 0 for Eq. (3).

Although the formation of cross-bridges is initiated by the binding of Ca^{2+} to TnC, attached cross-bridges have been shown to remain attached even after the Ca^{2+} detaches from the TnC. As the contractile force generated by muscle is proportional to the number of 'attached' cross-bridges, the following two states belong to the force-generating populations: 1) TnC binds with Ca^{2+} and cross-bridge is attached (O), 2) TnC does not bind with Ca^{2+} but cross-bridge remains attached (O'). In addition, the following two states are defined: 3) TnC binds with Ca^{2+} but cross-bridge is detached (U), and 4) TnC does not bind with Ca^{2+} and cross-bridge is detached (U'). The complete system can be represented by evolutionary equation in the matrix form as follows:

$$\begin{bmatrix} \dot{U}' \\ \dot{O}' \\ \dot{U} \\ \dot{O} \end{bmatrix} = \begin{bmatrix} -[\text{Ca}^{2+}]_f \cdot k_1 & k'_d \\ 0 & -[\text{Ca}^{2+}]_f \cdot k_2 - k'_d \\ -[\text{Ca}^{2+}]_f \cdot k_1 & 0 \\ 0 & [\text{Ca}^{2+}]_f \cdot k_2 \end{bmatrix} \begin{bmatrix} U' \\ O' \\ U \\ O \end{bmatrix} + \begin{bmatrix} k_3 & 0 \\ 0 & k_4 \\ -(k_a + k_3) & k_d \\ k_a & -(k_a + k_d) \end{bmatrix} \begin{bmatrix} U' \\ O' \\ U \\ O \end{bmatrix}, \quad (4)$$

where $[\text{Ca}^{2+}]_f$ is the concentration of free calcium given by Eq. (3) and $K_1, K_2, K_3, K_4, K_a, K_d$, and K'_d are the constants that determine the transition rate between the states⁽¹¹⁾. The force is given as the sum of the populations in two attached states:

$$F = [O] + [O']. \quad (5)$$

The calculated time courses of normalized membrane potential $x_N = x/x_{\max}$ in FHN model, $[\text{Ca}^{2+}]_f$, and F are shown in Fig. 1. In this simulation, F was modified so as to include the shortening deactivation⁽²⁶⁾ due to the ejection of blood starting at 0.1 sec.

2.3 Constitutive equation of cardiac muscles

To characterize the property of cardiac muscles, we adopted the Lin-Yin model⁽²⁵⁾ for the constitutive

Fig. 1 FHN, $[\text{Ca}^{2+}]_f$ and force histories

equation, which is an approach based on the hyperelastic material theory. A hyperelastic material is defined as a material having an elastic potential W , that is independent of the deformation paths. A stress tensor is derived by differentiating W with respect to the conjugate strain tensor. In the Lin-Yin model, W is divided into two components: one is passive (W_{pass}), and the other is active (W_{act}):

$$W_{\text{pass}} = c_1(e^q - 1), \quad (6)$$

$$Q = c_2(I_1 - 3)^2 + c_3(I_1 - 3)(I_4 - 1) + c_4(I_4 - 1)^2, \quad (7)$$

$$W_{\text{act}} = c_5 + c_6(I_1 - 3)(I_4 - 1) + c_7(I_1 - 3)^2 + c_8(I_4 - 1)^2 + c_9(I_1 - 3) + c_{10}(I_4 - 1). \quad (8)$$

In the above equations, I_1 and I_4 are defined as $I_1 = \text{tr } \mathbf{C}$ and $I_4 = \mathbf{N} \mathbf{C} \mathbf{N}$, where $\mathbf{C}$ is right Cauchy-Green deformation tensor, and $\mathbf{N}$ a unit vector defining the preferred direction of muscle fibers in the undeformed state. Under the assumption of incompressibility, the second Piola-Kirchhoff stress is derived as follows:

$$S_{ij} = -p(\mathbf{C}^{-1})_{ij} + 2 \frac{\partial W}{\partial C_{ij}} = -p(\mathbf{C}^{-1})_{ij} + 2 \left(\frac{\partial W_{\text{pass}}}{\partial C_{ij}} + \frac{\partial W_{\text{act}}}{\partial C_{ij}} \right), \quad (9)$$

$$= -p(\mathbf{C}^{-1})_{ij} + 2 \left(\frac{\partial W_{\text{pass}}}{\partial I_1} \frac{\partial I_1}{\partial C_{ij}} + \frac{\partial W_{\text{act}}}{\partial I_1} \frac{\partial I_1}{\partial C_{ij}} + \frac{\partial W_{\text{pass}}}{\partial I_4} \frac{\partial I_4}{\partial C_{ij}} + \frac{\partial W_{\text{act}}}{\partial I_4} \frac{\partial I_4}{\partial C_{ij}} \right). \quad (10)$$

As mentioned above, because the mechanical property of the cardiac muscle varies depending on the population of the attached cross-bridges, F , we considered the coefficients for active components, $c_5 \sim c_{10}$, to be a function of F , whereas those for passive components, $c_1 \sim c_4$, to be constants. The phasic change in stress-strain relationship during the cardiac cycle coefficients was modeled by setting

$$c_5 = F_R c_5^{\max}, c_6 = F_R c_6^{\max}, c_7 = F_R c_7^{\max}, c_8 = F_R c_8^{\max}, c_9 = F_R^2 c_9^{\max}, c_{10} = F_R^2 c_{10}^{\max}, \quad (11)$$

where F_R is the relative force as defined by $F_R = F/F_{\max}$. In Fig. 2, the reproduced stress-strain relationships are shown for various F_R .

3. Mechanical Model of LV

3.1 Fluid-structure interaction analysis

We cite some principal formulations below. For

Fig. 2 Stress-stretch relationship

precise formulation of FSI FE analysis, see Zhang and Hisada⁽²⁷⁾.

The ALE method is utilized for deformable fluid domains. We assume the viscous fluid to be isothermal and that $\partial P/\partial \rho = B/\rho$, with B , P and ρ being the fluid bulk modulus, the pressure, and the fluid density, respectively. The ALE form of the Navier-Stokes equations can be expressed as

$$\frac{1}{B} \frac{\partial P}{\partial t} \Big|_x + \frac{1}{B} c_i \frac{\partial P}{\partial x_i} + \frac{\partial v_i}{\partial x_i} = 0 \text{ in } R_t^f, \quad (12)$$

$$\rho \frac{\partial v_i}{\partial t} \Big|_x + \rho c_j \frac{\partial v_i}{\partial x_j} = \frac{\partial \sigma_{ij}}{\partial x_j} + \rho g_i \text{ in } R_t^f, \quad (13)$$

where $\partial(\cdot)/\partial t|_x$ is the time derivative in the ALE coordinates, the velocity of which is $\mathbf{v}_m$, and the convective velocity $\mathbf{c} = \mathbf{v} - \mathbf{v}_m$. σ is the Cauchy stress and $\mathbf{g}$ the acceleration of gravity. R_t^f denotes the spatial domain with the boundary ∂R_t^f at time t . The superscript f stands for the fluid component. The fluid is assumed to be Newtonian. Using the Galerkin method and spatial discretization for Eqs.(12) and (13), we obtain the following equations in the matrix form:

$$M^P \cdot \dot{P} + \Lambda^P \cdot P + G^T \cdot V = 0, \quad (14)$$

$$M \cdot \dot{V} + \Lambda \cdot V + K_\mu \cdot V - G \cdot P = F, \quad (15)$$

where M^P and M are the generalized mass matrices for pressure and velocity, respectively, and Λ^P and Λ are the generalized matrices of convective terms for pressure and velocity, respectively. K_μ is the fluid viscosity matrix, G is the divergence operator matrix, $\dot{P}$ and $\dot{V}$ are the time derivatives of the pressure and velocity vectors, respectively, in the ALE coordinates, and F is the external force vector.

Let R_t^s be the spatial domain of a structure. Here the superscript s stands for the structural component. The equilibrium equations for structure are:

$$\rho \frac{d^2 u_i}{dt^2} = \frac{\partial \sigma_{ji}}{\partial x_j} + \rho^s g_i \text{ in } R_t^s. \quad (16)$$

Upon total Lagrangian formulation and finite element discretization, a nonlinear system of equations is obtained in the matrix form, and the incremental form at each time step is given as follows:

$$M \Delta \dot{U} + {}^t K \Delta U = {}^{t+\Delta t} F - {}^t Q^s. \quad (17)$$

Here, M is the mass matrix, K the tangent stiffness matrix, and F the external force vector. Q^s is composed of the internal force and the inertial force of the structure, and $\Delta \dot{U}$ and ΔU are the increments of the acceleration vector and the displacement vector, respectively.

The full interaction conditions between the fluid and structure are introduced, i.e., the geometrical compatibility conditions:

$$v_i^f = v_i^s \quad (i=1, 2, 3) \text{ in } \partial R_t^c \quad (18)$$

and the equilibrium conditions:

$$\sigma_{ji}^f n_j^f + \sigma_{ji}^s n_j^s = 0 \quad (i=1, 2, 3) \text{ in } \partial R_t^c \quad (19)$$

are given, where n^f and n^s are the outward normals corresponding to the fluid and the structure, respectively, and ∂R_t^c is the interface between the fluid and the structure.

Based on the interface conditions described above, the fluid and the structure are coupled by equating the displacement, velocity and acceleration on the interface common to the fluid and the structure. The equilibrium on the interface is automatically enforced through the element assemblage process. Thus, the system equations in the strong coupling method are constructed and the incremental form can be expressed as

$${}^t M^{fs} \Delta \varphi^{fs} + {}^t C^f \Delta \varphi^{fs} + {}^t K^s \Delta U^s = {}^{t+\Delta t} F - {}^t Q^{fs}, \quad (20)$$

where φ^{fs} and U^s are the variable vectors of the coupled system, as defined by

$$\varphi^{fs} = \begin{Bmatrix} P \\ V_i^f \\ V_c \\ V_i^s \end{Bmatrix}, \quad U^s = \begin{Bmatrix} - \\ - \\ U_c \\ U_i^s \end{Bmatrix}. \quad (21)$$

Here, P is the pressure vector of the fluid, V_i^f the velocity vector of the fluid independent of the structure, V_c the coupled velocity vector, V_i^s the velocity vector of the structure independent of the fluid, U_c the coupled displacement vector, and U_i^s the displacement vector of the structure independent of the fluid. In Eq. (20), F denotes the external force vector of the coupled system and Q^{fs} the equivalent internal force vector including all effects. M^{fs} denotes the mass matrix composed of those for the fluid and the structure. C^f consists of the divergence, viscous and convective terms of the fluid. K^s is the tangent stiffness matrix of the structure.

Considering the numerical analysis of the heart, the boundaries of the fluid are assumed to consist of open boundaries and the interface with a deformable structure. Under these boundary conditions, the following methods are employed for mesh control in the fluid domain.

The mesh is fixed in space for open boundaries, i.e., $\mathbf{v}_m = 0$ is used. On the interface with a deformable structure, fluid nodes are attached to the structure,

Fig. 3 FE mesh and boundary conditions

i.e., the Lagrangian motion is assumed as $\mathbf{v}_m = \mathbf{v}_m^s$ where $\mathbf{v}^s$ is the velocity vector of the structure. In other words, the ALE coordinates are set to be identical to the Lagrangian coordinates on the deformable interface.

For the time integration method, the extended predictor-multicorrector algorithm is employed based on the Newmark- β time integration scheme, where $\beta=0.6$ and $\gamma=0.3025$ are used.

3.2 Windkessel model

To simulate the systemic arterial tree, the windkessel model⁽²⁸⁾ characterized by the following equations was used (see Fig. 3).

$$P = P_1 + P_2 \quad (22)$$

$$q = \frac{P_1}{R_1} \quad (23)$$

$$q = q_R + q_C = \frac{P_2}{R_2} + C \frac{dP_2}{dt} \quad (24)$$

P is aortic pressure, q blood flow, R_1 characteristic impedance, R_2 peripheral resistance, and C capacitance. In this paper, the following values are employed for these parameters: $R_1=1.0 \text{ E}+6 \text{ Pa sec/m}^3$, $R_2=150. \text{ E}+6 \text{ Pa sec/m}^3$, and $C=1.6 \text{ E}-8 \text{ m}^3/\text{Pa}$.

3.3 "Structural only analysis"

By neglecting the inertias of both fluid and structure and the fluid dynamics, the FSI program was reduced to a static structural FEM code that models only the cardiac muscles. This analysis will be termed "structure only analysis" hereafter. In phases 1 and 3, LVP is increased or decreased due to the change of the cardiac muscle state while LVV is kept constant. In phase 2, the flow through the windkessel model is calculated by the volume change of LV, and the pressure calculated by the windkessel model is applied to the structure as external forces. The equilibrium state of both structure and windkessel model is determined by iterative calculation. In phase 4, the LVV history is determined by the prescribed flow pattern as mentioned later. In all phases, the instantaneous LVV must be computed, and this was made possible by utilizing the fluid FE mesh generated for FSI analysis.

4. Numerical Examples

The following boundary and initial conditions were set for phases 1, 2, 3, and 4: During phase 1, both mitral and aortic valves are closed so that zero velocity is prescribed at those two boundaries. The initial value of LVV is 120 ml, LVP is 1500 Pa, and all cardiac muscles are in the resting state. Then, the muscles are activated by the excitation-contraction mechanism (represented by the FHN model and the four-state model) to increase the LVP. When the LVP exceeds the aortic pressure calculated by the windkessel model, the aortic valve opens. During phase 2; while the mitral valve is closed, the pressure boundary condition modeled by the windkessel model is applied to the open aortic valve area. FSI/structure only FE model and the windkessel model are iteratively calculated to determine the equilibrium state, and when backward flow occurs, the aortic valve is closed to finish phase 2. During phase 3, the relaxation of cardiac muscles proceeds while both the aortic and mitral valves are closed. When the LVP falls below the left atrial pressure (LAP, set at 20 mmHg in this analysis), the mitral valve opens and phase 4 begins. Instead of modeling the complex function of LA (conduit, reservoir, and pump), in this analysis, a typical flow velocity pattern as shown in Fig. 3 is applied as the boundary condition at the mitral valve. The mitral flow pattern consists of two peaks, the first one, called rapid filling, is caused by the cooperative action of LV relaxation and the right ventricular pump, whereas the second one is caused by the active contraction of LA. As is shown in clinical study, the first peak velocity is higher than the second one in young adults, so the ratio was set at about 3/2 in this analysis. Referring to the MR imaging data by Kilner et al.⁽²⁹⁾, the direction of the velocity is tilted toward the lateral wall by 10 degrees relative to the long axis of LV.

5. Initial Shape of LV and FE Mesh

Although it is a requirement for FE analysis to determine the LV mesh (initial shape) for its undeformed state under zero stress, we found it difficult to know the initial shape of a living human LV. Accordingly, we estimated it based on the following assumptions and procedures: 1) We tried to model the adult human LV, the volume of which is 120 ml, when LVP is 1500 Pa under fully relaxed condition (at end diastole). 2) It has been shown that if phase 3 (isovolumic relaxation) is forced to proceed at ESV, LVP becomes negative to reach the negative part of the end-diastolic pressure volume relationship. Since the ESV is about 40 to 45 percent of the EDV for normal

LV, we assumed the initial LVV (LVV at which LVP is 0 Pa) to be slightly larger than this value, i.e., 60 ml. To make FE mesh of LV whose LVV is 60 ml, the initial mesh was generated from the MR images of adult human LV at end diastole, and then modified by applying an appropriate negative pressure. The resultant FE mesh is shown in Fig. 3. In this paper, the 8/1d (eight nodes for the bilinear velocity or displacement interpolation/the constant pressure field) mixed hexahedral elements are used for both the fluid and the structure. The number of fluid elements is 2 372, that of solid elements 1 224 and total NDOF is about 15 000.

Another structural aspect should also be taken into consideration. The ventricular wall consists of multiple layers of muscle bundles following a spiral path from the ventricular base to the apex⁽²⁾. In this analysis, the ventricular wall was divided into three layers, i.e., endocardiac, middle and epicardiac layers, the fiber directions of which are -60° , 0° , and 60° degrees, respectively, relative to the plane perpendicular to the long axis of LV.

To stabilize blood flow ejected from LV, a short segment of outflow tract is also modeled as shown in Fig. 3, which is connected to LV at an angle of 40° degrees with respect to the long axis of LV, referring to the MR imaging data by Kilner et al.⁽²⁹⁾

In the electro-physiological analysis, the same structural mesh is employed, i.e., each solid element is taken as an electro-physiological unit. Thus, the excitation of one element conducts to surrounding elements. Isotropic conduction is assumed.

6. Material Properties

The coefficients in the passive part of the Lin-Yin model (c_1 to c_4) were determined so that the LVV becomes 120 ml when LVP is 1 500 Pa (11 mmHg) under the relaxed condition. This was achieved by using 80% of the average value given by Lin and Yin⁽²⁵⁾. The coefficients in the active part (c_5 to c_{10}) were determined to meet the following conditions: 1) Isolated unloaded cardiac myocytes contract up to 20%. 2) The maximum value of the time derivative of the LVP is between 200 kPa/sec (1 500 mmHg/sec) and 240 kPa/sec (1 800 mmHg/sec) in phase 1. First, we determined c_{10} to fulfill the contraction condition. Then, $c_5 \sim c_9$ were determined to achieve the expected time derivative values. The coefficients thus determined are as follows: $c_1 = 0.823\,76\,E+2$ Pa, $c_2 = 7.304$, $c_3 = 1.856$, $c_4 = 0.064$, $c_5^{\max} = 0.0$, $c_6^{\max} = -0.006\,389\,032\,E+6$, $c_7^{\max} = 0.017\,970\,686\,E+6$, $c_8^{\max} = 0.017\,367\,577\,E+6$, $c_9^{\max} = 0.007\,609\,96\,E+6$, $c_{10}^{\max} = 0.019\,422\,25\,E+6$. In addition, the density of cardiac muscle is given by $\rho = 1.366\,E+3$ kg/m³, the density of blood $\rho = 1.06$

Fig. 4 Pressure-volume loop

$E+3$ kg/m³, and viscosity $\mu = 4.71\,E-3$ Pa

6.1 Simulation for normal contraction

In the case of normal contraction, the excitation from the atrium spreads rapidly over the entire endocardium via the conduction system (Purkinje fibers) and then propagates toward the epicardium in a short period of time (40 m seconds)⁽²⁾. In this analysis, the stimulation is imposed on all elements in the endocardium with a duration of 50 m seconds and Eqs. (1) and (2) are solved with the following initial values and coefficients: $x = 1.2$, $y = 0.624$, $a = 0.7$, $b = 0.8$, $c = 0.7$, $g = 1.0$, and $z = 20$.

Three cycles of contractions were simulated assuming a heart rate of 60 per minute (one cardiac cycle = 1.0 sec). The propagation of excitation and the intra-ventricular flow pattern shown in Appendix 1 are in good agreement with the clinical observation. Detailed presentation of the results in the form of LV pressure-volume (P-V) loops (Fig. 4) and the time courses of LVP, AP, and three sampling points near the base, middle, and apex of LV (Fig. 5) raise some interesting issues. First, the resultant LVP in FSI analysis is higher than that in structure only analysis. FSI analysis also shows the spatial distribution of pressure in the LV caused by intra-ventricular flow motion. Notably, FSI analysis shows that during phase 2, LVP is higher than AP in the beginning but AP exceeds LVP in the later phase while the ejection continues. This phenomenon has been reported in animal experiments and was considered to be caused by the inertia of the blood⁽³⁰⁾. As shown in Fig. 6(a), comparison of the ejection flows determined by FSI and structure only analyses also demonstrated the effect of inertia, i.e., the peak in FSI analysis comes later than that in structure only analysis. Third, oscillations in LVP appear in FSI analysis. Because of the fiber orientation of the LV wall, torsional

Fig. 5 Pressure history

Fig. 6 Flow, rotation, and vertical displacement histories

deformation is generated during contraction. We quantified this by taking the average of the rotation of the points in cross section A (see Fig. 3), which is normal to the long axis (see Fig. 6(b)). As is shown in Fig. 6(b), during contraction, LV is twisted counterclockwise first, then twisted in the clockwise direction while oscillating fairly rapidly (20 Hz). Because damping was not introduced to the LV wall in the present FSI analysis, the oscillations appear slightly large. Figure 6(c) compares the vertical displacements of the apex (length change of the ventricle)

(b) Longitudinal direction

Fig. 7 Strain history

Fig. 8 Stress-stretch loops (fiber direction)

obtained by the two methods. Oscillations are again obtained in FSI analysis, but the displacement time course will not coincide with that of structure only analysis even if damping is introduced.

Because the issue of wall stress and strain has attracted the interest of researchers, the time courses of wall stretch in both fiber and longitudinal directions (Fig. 7(a), (b)) and the stress-stretch loops (Fig. 8) in fiber direction of sampling point B (see Fig. 3) are investigated. Figure 7(b) shows that the structure only analysis gives a much smaller estimation of the longitudinal stretch (about half in terms of strain) than FSI analysis during phase 4. This is because in FSI analysis, the LV wall is elongated in the longitudinal direction by the momentum of the filling fluid. Also, contrary to our expectations, the highest stress was observed in the middle layer. The reason for this is that while obliquely running fibers in endocardial and epicardial layers absorb stress by rotation, stretch is directly applied to the mid wall fiber running horizontally.

6.2 Arrhythmia

Although various types of arrhythmia should be investigated, in this study, we simulated the

Fig. 9 Pressure-volume loops (arrhythmia)

ventricular extrasystole⁽²⁾ as an example. In this setting, premature excitation starts from a small region in the ventricular wall (point A, Appendix 2), and then spreads slowly (in 200 m seconds) over the entire LV in a concentric manner. The stimulation was applied to eight elements around C in Fig. 3 with a duration 50 m seconds and the calculation was performed with the following parameters: $x=1.2$, $y=1.2$ and 0.624 , $a=0.7$, $b=0.8$, $c=0.7$, $g=2.2$, and $z=20$. Again, the aortic valve is supposed to open when LVP exceeds the AP modeled by the windkessel model, and during diastole, filling velocity similar to that of the normal case is given as the boundary condition.

The propagation of excitation and the intra-ventricular flow pattern are shown in Appendix 2. Also shown are the P-V loops (Fig. 9). These results well reproduced the clinical observation that reflects the insufficient filling and asynchronous excitation. The only exception was the relatively small ESV (suggesting fairly good contractility), because of the absence of a force-interval relationship⁽³¹⁾ in the present model.

7. Conclusions

To simulate the contraction of human LV and the associated blood motion, a 3D fluid-structure interaction FE code was developed. The results of the simulation in the cases of both normal excitation and arrhythmia could well reproduce the clinical observation. Comparison with the results obtained by the structure only analysis showed the importance of the fluid-structure analysis for the simulation of the heart, and the structure only analysis was found to give a fairly good approximation of some responses. Currently, we are attempting to improve the model by incorporating 1) damping of cardiac muscle, 2) fluid and structural dynamics of the left atrium, 3) a more

realistic electrophysiological model such as the LR model, and 4) the refinement of mesh for analysis of electrophysiology, fluid, and structure.

With these improvements, this model can truly be a useful tool for the study and care of the heart disease.

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Appendix 1: Normal Excitation

Appendix 2: Arrhythmia