論 文 内 容 要 旨

Interests in prevention and early detection of arteriosclerosis are growing in recent years. Extensive research on arteriosclerosis has shown that it is closely related to hemodynamics. Understanding detailed and accurate information on hemodynamics is essential for clarification of the pathogenic mechanism of arteriosclerosis. In recent years, blood flow measurement methods for acquisition of information on hemodynamics are diversified, and various methods are selectable according to a measurement object and a use. However, the existing measurement methods of medical imaging have difficulties in obtaining the detailed information on blood flow such as the pressure distribution and the wall shear stress in a blood vessel. On the other hand, a numerical simulation of blood flow based on the measurement data of the blood flow and the blood vessel shape by MRI and CT came to be popular to acquire a detailed structure of the blood flow. However, when dealing with circulatory system, it is essentially difficult to reproduce a real blood flow correctly because of the difficulty in specifying the computational conditions such as boundary conditions and physiological parameters. In order to complete the problems of a measurement and a calculation and to reproduce an intravascular blood flow field correctly, an ultrasonic-measurement-integrated (UMI) simulation has been developed. In UMI simulation a difference between measured and computed Doppler velocities is fed back to a flow simulation to compensate the discrepancy of measurement and computation (see Fig. 1(a)). This method correctly and efficiently reproduces the blood flow field and hemodynamics in a blood vessel such as wall shear stress (WSS) (see Fig. 1(c)) and pressure distribution corresponding to ultrasonic measurement data (see Fig. 1(b)).

In spite of existing studies for UMI simulations, there are problems to be solved for medical applications. Estimation of inflow velocity for the upstream boundary condition in 2D-UMI simulation is critically important for the accuracy of analysis
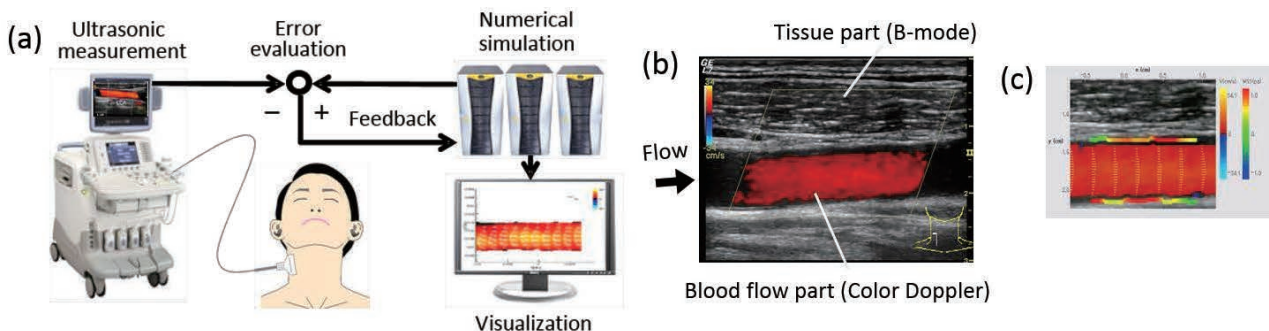
Fig. 1　(a) 2D-UMI blood flow analysis system, (b) ultrasonic measurement data, and (c) 2D-UMI blood flow analysis result.

result. There has been no systematic study for the validity of existing estimation methods. Effect of speckle noise in a real ultrasound Doppler velocity measurement on the accuracy of UMI simulation has not been investigated. Doppler velocity error was used to evaluate the analysis accuracy in existing studies of UMI simulation. Validation based on the velocity vector of blood flow is essential to confirm the validity of the UMI simulation.

The purpose of this dissertation was to establish analysis algorithms for the 2D-UMI blood flow analysis system to perform accurate analysis of blood flow and hemodynamics applicable to a wide variety of subjects in clinical sites. Specifically, optimization of the estimation method of inflow velocity and optimization of 2D-UMI analysis method considering the speckle noise in Doppler velocity data were investigated. Validation of analysis result based on velocity vector of blood flow was also done. In optimization of the estimation method of inflow velocity, a numerical experiment was performed to examine the validity of the existing methods to estimate an unsteady inflow velocity in 2D-UMI simulation for intravascular blood flow analysis and to propose a new estimation method applicable to various vessel geometries and flow conditions. In optimization of 2D-UMI analysis method considering the speckle noise in Doppler velocity data, ultrasonic measurements and two-dimensional ordinary (2D-O) and 2D-UMI analyses were performed by the 2D-UMI blood flow analysis system for steady and unsteady flows in a circular pipe in downstream of a stenosis. Evaluation of the results was carried out based on the instantaneous and frame-averaged Doppler velocity measurement data. The optimum feedback gain minimizing the error of the Doppler velocity of the 2D-UMI analysis result with respect to that of the frame-averaged measurement result was determined. Accuracy of frame-averaged analysis result was also clarified. As to validation of analysis result based on velocity vector of blood flow, 3D-CFD analysis was performed on the condition of the experiment, and the velocity vector fields of 2D-O and 2D-UMI analyses were evaluated by comparing with that of 3D-CFD result.

The major findings in the preset dissertation are summarized as follows.

Chapter 2 dealt with the optimization of the estimation method of inflow velocity. In this chapter, the validity of the existing methods to estimate an unsteady inflow velocity in 2D-UMI simulation for intravascular blood flow analysis was systematically investigated, and a new estimation method applicable to various vessel geometries and flow conditions was proposed. A numerical experiment was performed for the 2D-UMI simulation of blood flows in a simple straight blood vessel model with inflow velocity profiles symmetric and asymmetric to the vessel axis using two existing evaluation functions for the inflow velocity estimation: the average value of the errors of Doppler velocities and the error of the average values of Doppler velocities.

In case of a simple straight blood vessel model, it was clarified that a significantly large estimation error of 35% occurs in the asymmetric flow due to nonreduced velocity vector error in spite of reduced Doppler velocity error for 2D-UMI simulation which has a nonfeedback domain near the downstream end. In order to remove the effect of the downstream nonfeedback domain, a new inflow velocity estimation method in which the feedback domain is extended to the downstream end was proposed. This estimation method resulted in small estimation error of 2% and a reasonable result of flow field close to the standard solution (see Fig. 2). A further numerical experiment of 2D-UMI simulation for two realistic vessel geometries of a healthy blood vessel and a stenosed one confirmed the effectiveness of the proposed method. Moreover, the superiority of the evaluation function with the average value of the errors of Doppler velocities to that of the error of the average values of
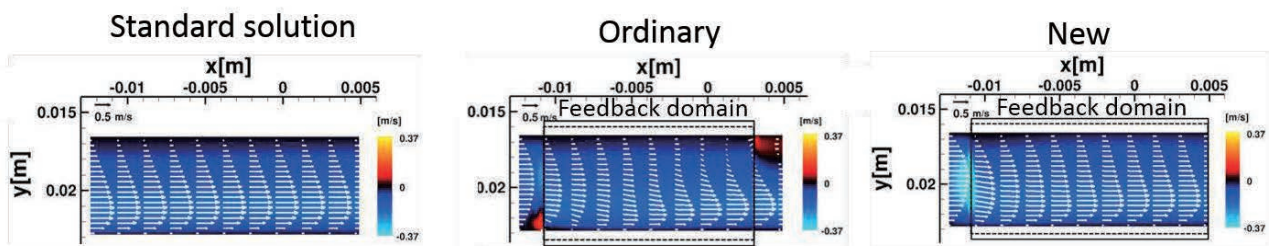

Fig. 2   Velocity vectors and Doppler velocity distribution of asymmetric standard solution, 2D-UMI simulation for ordinary evaluation function, and that for new one.

Doppler velocities was confirmed. The former is more sensitive to the difference between the result of 2D-UMI simulation and the standard solution than the latter since the latter evaluates the error in the whole domain and some errors at different grid points can cancel each other out.

Chapter 3 dealt with the optimization of 2D-UMI analysis method considering the speckle noise in Doppler velocity data. The study in this chapter clarified the effect of speckle noise in ultrasonic measurement on 2D-UMI blood flow analysis system. Ultrasonic measurements and 2D-O and 2D-UMI analyses were performed by the 2D-UMI blood flow analysis system for steady and unsteady flows in a circular pipe in downstream of a stenosis. Evaluation of the results was carried out based on the instantaneous and frame-averaged Doppler velocity measurement data. The optimum feedback gain was determined by minimizing the error of the Doppler velocity of the 2D-UMI analysis result with respect to that of the frame-averaged measurement result, which is thought to be close to that of the real flow. Accuracy of frame-averaged analysis result was also clarified.

In an ultrasonic measurement experiment, the Doppler velocity distribution deflected to the lower side due to the upstream stenosis was obtained. Doppler velocity distribution without the effect of speckle noise was obtained by frame-averaging the measurement data, and the distribution of the speckle noise in the instantaneous Doppler velocity measurement was quantitatively shown. As for the velocity vectors and Doppler velocity distributions of the 2D-UMI analysis results, the velocity profile of the flow field deflected to the lower side due to the upstream stenosis is properly reproduced in the 2D-UMI simulation for $K_V^* = 110$ in the feedback domain (see Fig. 3(a)). Although the deflected velocity profile is also reproduced in the 2D-UMI simulation for $K_V^* = 500$, the velocity profile is rough, probably because the speckle noise of the measurement data is reproduced in the result (see Fig. 3(b)). Instantaneous Doppler velocity error $\bar{e}_{Vi}$, which was used in former studies to evaluate the UMI simulation ignoring the effect of measurement error, monotonically decreases with increasing feedback gain in 2D-UMI simulation (see Fig. 3(c)). Frame-averaged Doppler velocity error $\bar{e}_{Va}$, on the other hand, enables us to evaluate the accuracy of analysis result without the effect of measurement error. The frame-averaged Doppler velocity error $\bar{e}_{Va}$ without speckle noise was minimal at almost the same feedback gains of 110 and 100 in the 2D-UMI analysis for steady and unsteady flow conditions (see Fig. 3(d)). The optimum feedback gain was determined for actual ultrasonic measurement data as about $K_V^* = 100$. The result of 2D-UMI analysis with the optimum feedback gain was compared with that of frame-averaged result of 2D-UMI analysis with a higher feedback gain. It was confirmed that the latter shows a smaller Doppler velocity error but a degraded frequency response.

As to the reproducibility of the flow field, 2D-UMI analysis with the optimum feedback gain properly reproduced the steady flow deflected to the lower wall in downstream of a stenosis due to the Coanda effect, in which a jet flows along an obstacle by entrainment. 2D-UMI analysis with the optimum feedback gain also reproduced the unsteady flow consisting of uniform velocity profiles at initial and middle acceleration phases, almost parabolic profile at the fastest phase, and profiles deflected to the lower wall at deceleration phases.
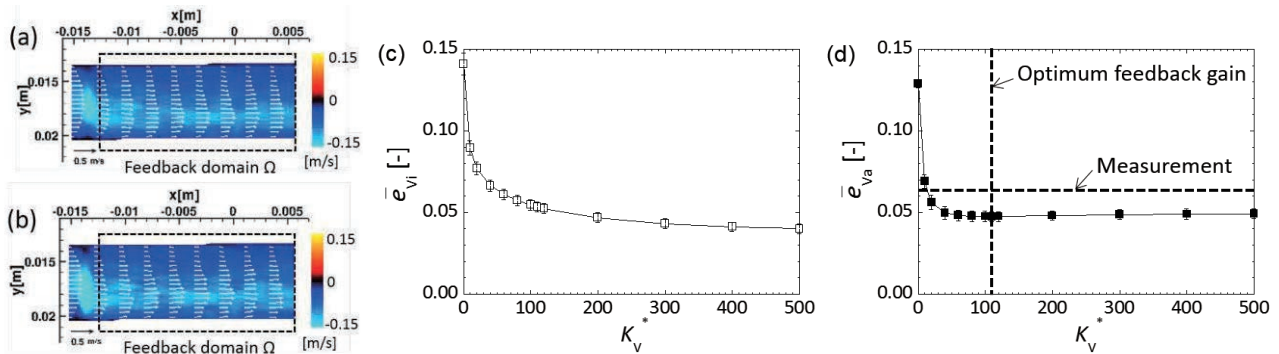

Fig. 3 Velocity vectors and Doppler velocity distributions for the analysis results for (a) $K_V^* = 110$ and (b) $K_V^* = 500$ for a steady flow, and variations of (c) the time-averaged value of the instantaneous-value-errors and (d) that of the averaged-value-errors with feedback gain.

Chapter 4 dealt with validation of analysis result based on velocity vector of blood flow. The study in this chapter was aimed to clarify the accuracy of velocity vectors in the results of 2D-UMI blood flow analysis system. Evaluation of velocity vectors was performed based on the analysis result of 3D-CFD corresponding to the ultrasonic measurement experiment. Target flow of the ultrasonic measurement experiment was a steady flow of blood-mimicking fluid in a circular pipe in downstream of a stenosis. The 2D-UMI analysis results for the ultrasonic measurement data obtained by the experiment were used. Accuracy of the two-dimensional velocity vectors of 2D-UMI blood flow analysis was evaluated by comparing with those of 3D-CFD analysis result in the ultrasonic measurement domain.

The (u, v) velocity vector field of 3D-CFD analysis result on the longitudinal section including the stenosis and measurement region is shown in Fig. 4(a). The developed laminar parabolic profile flow in the upstream side of the stenosis is accelerated in the stenosed part, and separates at the downstream side of the stenosis (A). After that, the flow re-attaches (B), deflects to the lower wall (C), and converges to the parabolic profile again (D). In comparison with 2D-UMI analysis result, it was clarified that the 2D-UMI blood flow analysis system properly reproduces the (u, v) velocity vector field of 3D-CFD analysis. The 73-frame-averaged 2D-UMI analysis results for $K_V{}^* = 110$ and 500 reproduce the u velocity profile of 3D-CFD analysis at the downstream side in the feedback domain within the error of 13% of the maximum u velocity of 3D-CFD result except for the region near the wall (see Fig. 4(b)). The u and v velocity profiles of 2D-UMI analysis are closer to those of 3D-CFD analysis toward the downstream side because of the feedback effect. The larger the gain becomes, the faster the velocity profiles converge to those of 3D-CFD analysis toward downstream, but the more the effect of speckle noise appears.

As to time variation of error, Doppler velocity error took the minimum at about $K_V{}^* = 100$, but instantaneous velocity vector error $\bar{e}_{\mathrm{ui\,ave}}$ did not take the minimum (see Fig. 4(c)). As to frame averaging, the variation of the velocity vector error with the number of frame averaging is small. This is probably because the speckle noise has little influence to the velocity vector error since the u-velocity of the 2D-UMI simulation is smaller than that of the 3D-CFD analysis in the whole domain.

In conclusion, analysis algorithms for the 2D-UMI blood flow analysis system to perform accurate analysis of blood flow and hemodynamics applicable to a wide variety of subjects in clinical sites was established by optimization of the estimation method of inflow velocity and optimization of 2D-UMI analysis method considering the speckle noise in Doppler velocity data. Validation of accuracy of velocity vector of blood flow was also done. These findings enable us to perform more accurate analysis of blood flow and hemodynamics.
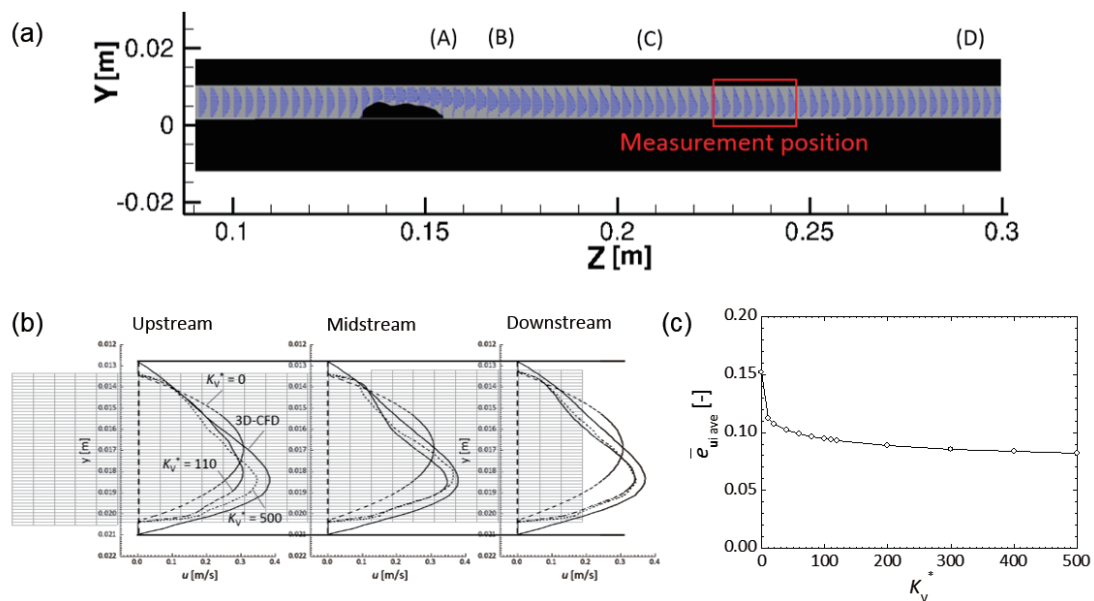

Fig. 4 (a) Velocity vectors near a stenosis of 3D-CFD analysis result, (b) velocity u of 73-frame-averaged values of 3D-CFD, 2D-O, and 2D-UMI analyses for $K_V{}^* = 110$ and 500 in measurement position, and (c) variation of time-space-averaged instantaneous value error of velocity vector with feedback gain.

論文審査結果の要旨

　循環器系疾患の機序の解明や新たな診断法の開発には詳細かつ正確な血流動態の取得が不可欠であるが，現在の医療画像計測手法や数値シミュレーション手法単独では取得が困難である。これらの手法が有する問題点を解決し，生体内の血流場を詳細かつ高精度に再現する方法として，超音波計測融合(UMI)シミュレーションがある。本手法に関してこれまで多くの研究がなされているが，臨床応用において重要な，上流端流速の推定手法や，超音波計測に含まれるスペックルノイズがUMIシミュレーションの解析精度に与える影響は未知である。また，UMIシミュレーションの解析精度はこれまで超音波ドプラ速度で評価されているが，実際の速度ベクトルによる評価は行われていない。本研究では，臨床用の2次元UMI(2D−UMI)血流解析システムにおいて，臨床現場での多様な対象に対して高精度な解析を可能とする解析アルゴリズムの確立を目的とし，2D−UMIシミュレーションの解析精度に大きな影響を与える上流端流速推定アルゴリズムの最適化と，スペックルノイズを含む実際の超音波ドプラ速度計測データを用いた2D−UMIシミュレーションにより高精度な解析結果を得るためのアルゴリズム最適化，および2D−UMIシミュレーションによる速度ベクトルの再現性の検証を行っている。本論文は，これらの研究成果についてまとめたもので，全編5章よりなる。

　第1章は序論であり，本研究の背景及び目的を述べている。

　第2章では，上流端流速推定アルゴリズムの最適化について検討している。従来の上流端流速推定手法に対して，種々の血管形状や流れ条件における系統的な数値実験を行って，2D−UMIシミュレーションの解析精度を明らかにし，高精度かつ汎用的な新たな上流端流速推定手法を確立している。これは，2次元UMI血流解析システムの臨床応用に不可欠な重要な成果である。

　第3章では，スペックルノイズを含む実際の超音波ドプラ速度計測データを用いた2D−UMIシミュレーションにより高精度な解析結果を得るためのアルゴリズム最適化について検討している。直円管内に設けた狭窄の下流の定常流実験により，実際のスペックルノイズを有する超音波計測データを用いた2D−UMIシミュレーションを行って，スペックルノイズの影響を考慮して高精度な解析結果が得られる最適ゲインの決定や，フレーム平均による高精度化アルゴリズムを確立している。これは，2次元UMI血流解析システムによる高精度解析の実現に不可欠な重要な成果である。

　第4章では，2D−UMIシミュレーションによる血流場の速度ベクトルの解析精度について検討している。直円管内に設けた狭窄の下流の定常流実験を再現した3次元数値流体解析結果との比較により，2D−UMIシミュレーションによる血流場の速度ベクトルの解析精度を明らかにしている。これは，2次元UMI血流解析システムによる血流動態の解明や高度診断法の実現に不可欠な重要な成果である。

　第5章は結論である。

　以上要するに，本論文は2D−UMI血流解析システムにおいて，臨床現場での多様な対象に対して高精度な解析を可能とする解析アルゴリズムの確立を目的とし，2D−UMIシミュレーションの解析精度に大きな影響を与える上流端流速推定アルゴリズムの最適化と，スペックルノイズを含む実際の超音波ドプラ速度計測データを用いた2D−UMIシミュレーションにより高精度な解析結果を得るためのアルゴリズム最適化，2D−UMIシミュレーションによる速度ベクトルの再現性の検証を行ったものであり，バイオロボテイクスおよび生体医療流体工学の発展に寄与するところが少なくない。

　よって，本論文は博士(工学)の学位論文として合格と認める。