Image-based Simulation of the Three-dimensional Coronary Blood Flow

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EXTENDED ABSTRACT

The best way to further improve the quality of care in the fields of interventional cardiology and coronary surgery is to devise a computer system that enables clinicians to quantitatively assess the patient's coronary hemodynamics and quantitatively predict the improvements in the perfusion of the myocardium that can be achieved with specific revascularisation measures.

We will describe the development of the key components of such a computer system that are intended to provide a basis for patient-specific simulation studies of the three-dimensional flow of blood in the coronary arteries, especially around sections with a stenosis (narrowing). Since stringent time limitations are imposed on our computational tasks, it is necessary to extensively exploit parallelism. Our computer system will be implemented within the framework of the newly-established "Austrian GRID", a GRID infrastructure with large-scale parallelism. Physicians at various sites within a given geographical region will have full access to these facilities.

We will give a brief overview of the medical background and the methods employed in the development of our system and then concentrate on patient-specific simulation studies of the three-dimensional blood flow around a stenosis which were done with the finite element method.

Patient-specific simulation studies must be based on medical images. This article is merely intended to provide an overview of the required image processing tasks, such as the segmentation of biplane angiograms and three-dimensional reconstruction. We will also, at least in outline form, give a preview of the planed co-registration and image fusion tasks of the three-dimensional reconstructed coronary arteries and 3D perfusion images of the myocardium.

The specific problems raised by the segmentation of the angiograms, the three-dimensional reconstruction and the generation of a high-quality mesh in the flow domain will be dealt with in more detail in the companion paper entitled "Imaging and Mesh Generation Issues in Patient-specific Simulation Studies of Coronary Hemodynamics" (Mayr and Quatember 2007).

1 INTRODUCTION

The crucial task of treatment planning in the field of coronary artery disease (CAD) has proven to be a rather challenging one. In this paper we will show that a multidisciplinary approach involving medical image analysis, mathematical modelling, and computer simulation can yield information of relevance for diagnosis. Our approach can help to improve the quality of care and will make a contribution to the lowering of the relatively high death rate from this disease. CAD results from the narrowing of the coronary (epicardial) arteries (Gould 1999; Zipes and Braundwald 2005). These vessels supply the myocardium (the muscle of the heart) with oxygen and nutrients (Lüdinghausen 2003a; Lüdinghausen 2003b). We usually distinguish between two kinds of narrowing: diffuse ones and stenoses (local narrowing). Such pathological changes to the flow domains of the blood may reduce the delivery of oxygen and nutrients to the myocardium. At advanced stages of CAD, the myocardium becomes vulnerable to ischemia. Moreover, the irregular flow pattern around the central region of a stenosis and downstream from it may induce the formation of thrombi and emboli and, in the worst case, cause a complete occlusion of coronary arteries (Fuster 2005).

All the therapeutic measures currently being employed (pharmacotherapy, bypass surgery, balloon angioplasty/stents) are intended to improve the geometry of the flow domain so as to increase the supply of blood to the myocardium (Buzug 2007; Meier 2004; Soper *et al.* 2005; Trahair 2002). The techniques of coronary surgery and interventional cardiology are already highly refined (Buzug 2007; Soper *et al.* 2005). In contrast, contemporary methods for making diagnoses and clinical decisions and for planning coronary interventions and surgery are much less advanced. Our simulation efforts are designed to enable clinicians to quantitatively assess the patient's impaired coronary hemodynamics and quantitatively predict the improvements in the perfusion of the myocardium that can be achieved with specific therapeutic (revascularisation) measures. They thereby help clinicians who are considering alternatives for the treatment of a patient and enable them to avoid unnecessary interventions. Furthermore, the simulation studies of the irregular 3D flow patterns and the flow-induced shear stress of the inner arterial wall will give cardiologist sufficient information about the conditions decisive for the further growth of the stenosis and the possible formation of thrombi and emboli.

There are two different modelling approaches (Arnez 2003; Ayache 2004; Kecman 1988; Ottesen and Danielsen 2000) available for our problem area (the simulation of the coronary hemodynamics), namely:

- The lumped parameter modelling approach and
- The distributed parameter modelling approach.

The lumped parameter modelling approach is sufficiently accurate to quantitatively simulate the overall flow in the coronary arteries and the supply of blood to the myocardium, but cannot be employed if, for instance, information about the three-dimensional flow pattern around a stenosis is required. In that case, the distributed parameter modelling approach must be chosen. This approach, however, is extremely expensive in terms of computing time, since it involves the solution of systems of partial differential equations. In contrast, the lumped parameter modelling approach only requires the solution of systems of ordinary differential equations (systems of differential algebraic equations) and is thus less expensive in terms of computing time.

Lumped parameter modelling approach: Due to the high complexity of the cardiovascular system, and especially the coronary network, the lumped parameter modelling approach is the only way to simulate the hemodynamics of the entire coronary system. In our approach, we will include a very detailed description of the network of the coronary vessels with a large number of lumped components; nevertheless, we only feel justified in making relatively rough approximations concerning the blood circulation in other regions. We also incorporate stenosed sections and, wherever applicable, bypass conduits into our lumped parameter models. In addition, the project will provide features that enable physicians to simulate pathological changes in the overall functional conditions of the circulation (e.g. tachycardia) and to study the effects of such changes upon coronary hemodynamics. The figure that is most significant for the diagnosis and planning of treatment is the time-variant volumetric rate of flow in the coronary capillary bed, since the exchange of oxygen, nutrients, and waste products with the myocardium takes place in this section of the coronary network. We would like to emphasize the fact that the coronary network is part of the circulatory system and thus cannot be modelled independently of the rest of the cardiovascular system.

Distributed parameter modelling approach: There are other important medical problems that require simulation models based on a distributed parameter modelling approach. One such problem area that to a significant extent depends on hemodynamic conditions is the assessment, therapy, and prevention of thrombotic and thromboembolic occlusions in diseased epicardial arteries, especially in ones with stenoses. To obtain relevant information, partial differential equations must be solved with the help of the finite element method.

Hence, a sufficiently fine mesh is needed for the entire flow domain. We always aim at creating one that is of such high-quality that it approximates an optimal one. The generation of such a mesh is a rather difficult task, since the geometry of the coronary arteries is highly complicated. This is particularly true if there are stenoses, but it is also pertinent if a diffuse narrowing (diffuse coronary artery disease) is present. Moreover, it is necessary to specify (initial and) boundary conditions.

In this paper, we will confine ourselves to the distributed parameter modelling approach, in particular to the simulation of the three-dimensional flow conditions in the coronary arteries. In the following, we will focus on simulations of the disturbed flow in a proximal section of a circumflex artery with a markedly eccentric stenosis.

2 SIMULATION OF THE DISTURBED THREE-DIMENSIONAL FLOW PATTERN IN THE REGION OF A STENOSIS

As adumbrated in the introductory remarks, there are specific medical problems that require simulation models produces with a distributed parameter modelling approach. A medical problem area that requires a fair knowledge of the three-dimensional pattern of the disturbed flow of blood around stenoses is, for instance, the risk assessment and prevention of thrombotic and thromboembolic events.

2.1 Governing equations and their solution with the finite element method

We consider the flow of blood within the entire flow domain of the coronary arteries to be laminar.

Governing equations: As was mentioned earlier, these are the following kinds of partial differential equations:

- The continuity equation and
- The Navier Stokes equation.

For both of these, three-dimensional versions are employed. We solved these equations by using the finite element method. In doing so, we treated the blood as an incompressible and homogeneous non-Newtonian fluid which obeys the power law. Moreover, it is necessary to specify (initial and) boundary conditions. We presume ”no slip” conditions at the wall and ”natural” boundary conditions at the outlet. At the inlet, a paraboloid velocity profile has been assumed, which, however, is difficult to determine quantitatively, since our model merely describes the flow in one particular stenosed arterial section which is only one of many segments of the cardiovascular system. The authors of previous models of three-dimensional coronary flow in the domain of a stenosis made plausible assumptions but could not verify them. In contrast to all other contemporary modelling concepts, we aim at a solution that makes use of the above-mentioned lumped parameter modelling approach for the entire blood circulation system.

Geometry of the flow domain: We assumed a geometry typical for a proximal segment of a circumflex artery with a severe eccentric stenosis. We made simplifying hypothesis that all luminal cross-sectional areas along the entire arterial segment are ellipses. Figure 1 shows a wire-frame representation of the geometry of this diseased arterial segment; this figure also contains the required nodes for the generation of a mesh. Such a geometric model is called a meshable representation or an empty mesh of the flow domain (Quatember *et al.* 2005).

Mesh generation: We decided to use a structured mesh with hexahedral elements and adopted a multi-block meshing approach (Quatember and Mühlthaler 2003; Quatember *et al.* 2005). The ellipses in Figure 1 are regarded as elements which subdivide our arterial segment into individual blocks. In Figures 2 to 3, the central region of the stenosis in Figure 1 is magnified. Figure 2 refers to the state before the generation of the mesh. It was automatically produced block by block with a commercial mesh generator (GAMBIT). In Figure 3, the mesh in one block of the flow domain can be seen. By joining those of the individual blocks we obtain the final one that covers the entire flow domain under consideration (cf. Figure 4).

2.2 Simulation results

Our finite element computations of coronary hemodynamics yield a wealth of numerical data. However,

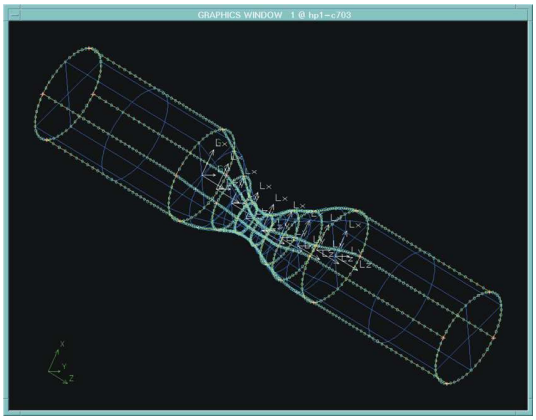

Figure 1. Meshable geometric representation of the flow domain (empty mesh) around an eccentric stenosis

Figure 2. Meshable geometric representation of the flow domain (empty mesh) around an eccentric stenosis (magnified)

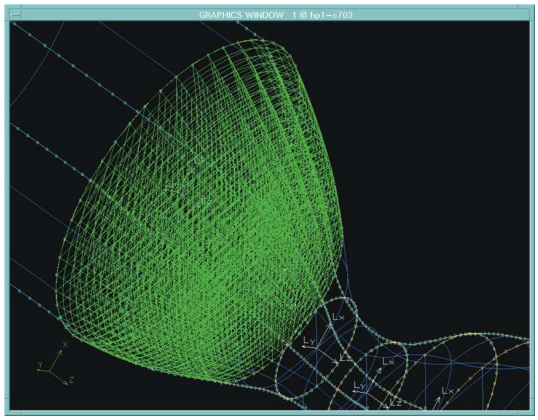

Figure 3. Generation of the mesh in one block of the flow domain (magnified)

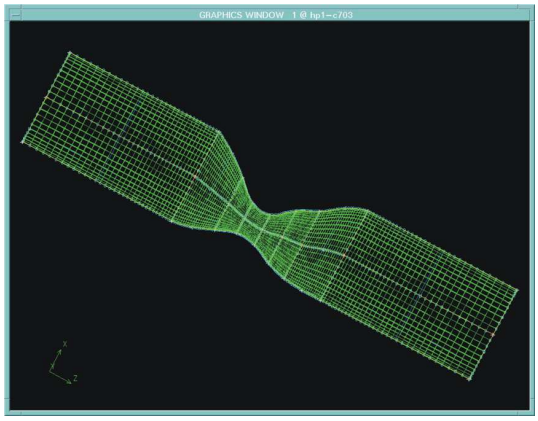

Figure 4. Mesh in the entire flow domain of the stenosed arterial section

excessively long lists of numerical data would be very difficult to comprehend and to analyse. For this reason, the simulation results are usually represented as surface plots, contour plots, fishnet plots, diagrams, and other graphics.

In the following, we present simulation results for our stenosed artery (circumflex artery). The contour plots in Figures 5 to 8 show the spatial variation of important fluid mechanical quantities in the central region of the stenosis under steady-state flow conditions at the end of the diastole. In these graphical representations, we used a three-dimensional Cartesian coordinate system (XYZ coordinates). The Z axis is the longitudinal axis of the stenosed artery, the X axis lies in the longitudinal cutting plane, where the stenosis reveals its greatest eccentricity. The simulation results in Figures 5 to 7 refer to a longitudinal cutting plane, namely the X-Z plane, whereas those of Figure 8 represent the spatial variations of the shear stress along the inner arterial wall. The fluid mechanical quantity presented in Figure 5 is the absolute value of the velocity (speed).

Figure 6 shows the spatial variation of the pressure. It is interesting to note that negative pressure values occur downstream from the apex of the stenosis.

In Figure 7, the spatial variation of the shear stress within the flow domain in a longitudinal cutting plane can be seen. This fluid mechanical quantity is of great importance for the behavior of the blood cells in our domain, where the flow is quite irregular. The shear stress influences "blood cell - vessel wall" interactions (reactions), which are relevant for the formation and the development of thrombi.

In Figure 8, the spatial variation of the flow-induced shear stress along the inner arterial wall (endothelium) is depicted.

The flow-induced wall shear stress distribution at the apex of our eccentric stenosis exhibits large spatial gradients which have a significant influence on specific pathophysiological processes.

3 IMPORTANCE OF PATIENT-SPECIFIC SIMULATION STUDIES

In the preceding section of this article, we assumed a geometrical conformation typical for a markedly eccentric stenosis in the circumflex artery. Hence, the simulation studies cannot be regarded as being patient-specific, since we have to bear in mind that interindividual anatomical variations of the coronary arteries do exist. To be of clinical value, simulation studies of the coronary hemodynamic must be carried out patient-specifically or, in other words, the simulation studies must be based on the

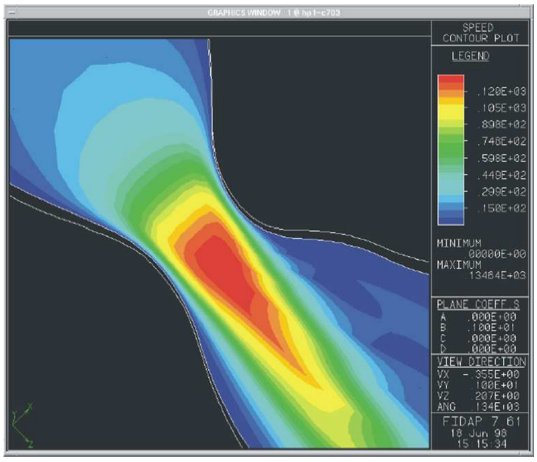

Figure 5. Contour plot of the variation of the absolute value of the velocity (speed) on the longitudinal cutting plane (X-Z plane); range: 0.00 cm/s to 69.17 cm/s

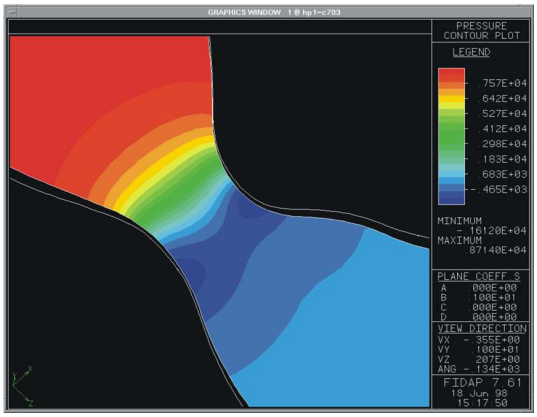

Figure 6. Contour plot of the variation of the pressure on longitudinal cutting plane (X-Z plane); range: -2586.3 dyn/cm2 to 13981.0 dyn/cm2

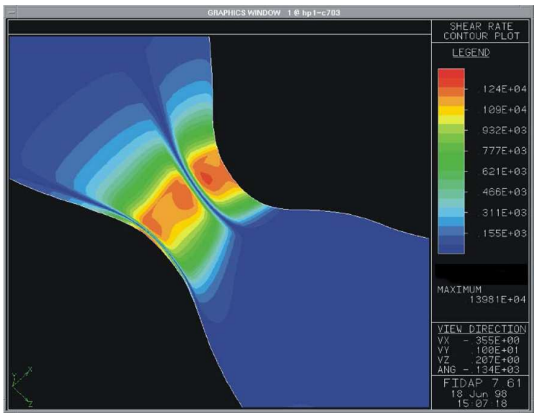

Figure 7. Contour plot of the variation of the shear stress in the flow domain on longitudinal cutting plane; range 0.00 dyn/cm2 to 48.93 dyn/cm2

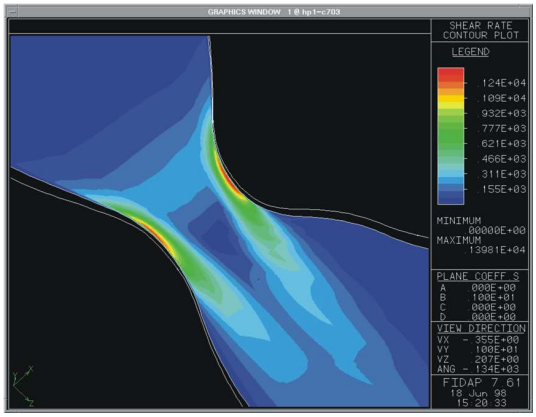

Figure 8. Contour plot of the variation of the flow-induced shear stress along the inner arterial wall; range 0.00 dyn/cm2 to 48.93 dyn/cm2

specific geometry of a particular patient's coronary arteries. It is thus necessary to acquire the necessary geometric data of the coronary arteries by taking medical images. At present, the preferred imaging modality for fulfilling this task is still biplane angiography (Rougee *et al.* 1994; Singh *et al.* 2006). The images are taken with biplane angiographic systems consiting of "X-ray tube - image intensifier" pairs. The X-ray tubes cast shadows of the coronary arteries that are filled with a contrast medium onto the image intensifiers. The resulting two images are called biplane angiograms. In both angiograms, the coronary artery tree must be segmented. Subsequently, its structure must be three-dimensionally reconstructed (Blondel *et al.* 2006; Mayr and Quatember 2007; Quatember and Mühlthaler 2003). In clinical settings the segmentation procedures as well as the three-dimensional reconstruction should be carried out (computed) entirely or or largely automatically. Furthermore, we must generate a high-quality mesh in the flow domain. We developed algorithms which handle this task largely automatically. Unfortunately, all these procedures are extremely expensive in terms of computing time and require the exploitation of parallelism. The segmentation tasks, three-dimensional reconstruction and the mesh generation algorithms are described in Mayr and Quatember (2007).

4 IMPLEMENTATION ASPECTS

Our software development efforts have not yet been completed. At present, the computational tasks are still being carried out with a single high-performance computer. However, in this way we will not be able to handle the more demanding and considerably more complex computations that will arise as the project progresses and as soon as the software is used in clinical settings. Moreover, we have also to bear in

mind that these complex computations must be carried out in a relatively short period of time, since clinicians cannot wait too long for the results.

Although some software modules are still under development, we have already made preparations to exploit the performance gains achievable with the "Austrian GRID", a newly-established GRID architecture which is supported by the Austrian Federal Government (Fahringer *et al.* 2006; Quatember *et al.* 2006). A further advantage of the GRID solution will be the easy access to medical databases and especially to picture-archiving and communication systems (PACS).

We aim at the establishment of an intelligent environment that is at the disposal of cardiologists and heart surgeons at various sites (hospitals) throughout an extended geographical region. This GRID-based infrastructure will give us standardised access to all necessary resources (computers with different architectures, storage media and input and output devices). The configuration of the "Austrian GRID" can be seen in the block diagram of Figure 9. The clusters of workstations within the "Austrian GRID" will primarily compute the image processing tasks, the mesh generation tasks and the simulation tasks which are based on lumped parameter models in parallel whereas the supercomputers in the GRID will carry out the three-dimensional simulations of the flow patterns (especially around stenoses) based on the finite element method (Quatember *et al.* 2006).

5 CONCLUSION AND FUTURE WORK

We have described simulation studies of the coronary hemodynamics, especially in the flow domain of a proximal arterial section of a circumflex artery. These studies are still subject to various restrictions. They are pertinent to the steady-state flow conditions at the end of the diastole. A typical geometric conformation of an arterial section with an eccentric stenosis has been assumed; hence the simulation results cannot be regarded as being patient-specific.

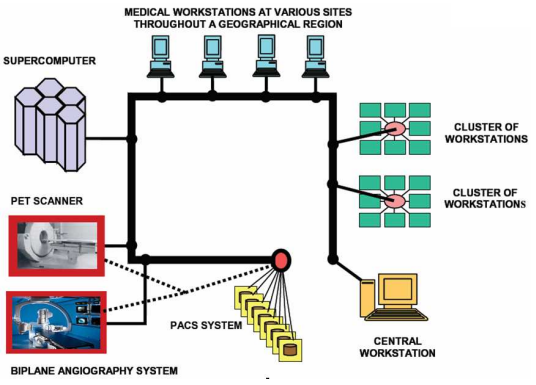

Figure 9. Configuration of the "Austrian GRID"

We have already developed methods and algorithms for the acquisition of the patient-specific three-dimensional geometry of the coronary arteries and have also carried out first patient-specific simulation studies which are described in Mayr and Quatember (2007), and we will continue our patient-specific modelling and simulation efforts.

We will refine our modelling approach by lifting most of the restrictions inherent in our present modelling techniques.

Furthermore, we plan to improve our modelling concepts, especially our lumped parameter modelling approach, by considering the possible formation of collaterals. Up to now, we have taken as granted that the coronary arteries have a strict tree-like structure, since this assumption is essentially true under physiological conditions. However, in coronary artery disease, an effective collateral vasculature may develop. It may then become possible to supply the primary perfusion territory of a severely obstructed or even occluded arterial segment with blood from another branch of the arterial tree via collateral conduits. We plan to extend our lumped parameter modelling approach by incorporating lumped components into the model which describe the flow of blood through the collateral conduits. The parameters of these lumped components can be determined on the basis of three-dimensional perfusion imagery (PET, SPECT, NMR).

6 ACKNOWLEDGEMENT

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7 REFERENCES

Arnez, Z. M. 2003. Simulations in biomedicine V. WIT Press, Computational Mechanics, Ashurst, Southampton, UK Billerica, MA.

Ayache, N. 2004. Computational models for the human body. Elsevier, Amsterdam.

Banerjee, R. K., Back, L. H., Back, M. R., and Cho, Y. I. 2003. Physiological flow analysis in significant human coronary artery stenoses. *Biorheology*, **40(4)**, 451-76.

Blondel, C., Malandain, G., Vaillant, R., and Ayache, N. 2006. Reconstruction of coronary arteries from a single rotational x-ray projection sequence. *IEEE Transactions on Medical Imaging*, **25(5)**, 653-63.

Buzug, T. M. 2007. Advances in medical engineering. Springer, Berlin ; New York.

Fahringer, T., Prodan, R., Trawoeger, B., Quatember, B., and Mayr, M. 2006. Workflow modelling of grid-based system for diagnosis of coronary artery disease with agwl. In J. Volkert, T. Fahringer, D. Kranzlmueller, and W. Schreiner, editors, *1st Austrian Grid Symposium*, **volume 210**, 234-244, Schloss Hagenberg, Austria, 2006. Oesterreichische Computer Gesellschaft (books@ocg.at).

Fuster, V. 2005. Atherothrombosis and coronary artery disease. Lippincott Williams & Wilkins, Philadelphia, 2nd edition.

Gould, K. L. 1999 Coronary artery stenosis and reversing atherosclerosis. Arnold, London etc., second edition.

Kecman, V. 1988. State-space models of lumped and distributed systems. Springer, Berlin etc.

Lüdinghausen, M. von. 2003. The clinical anatomy of coronary arteries. Springer, Berlin.

Lüdinghausen, M. von. 2003. The venous drainage of the human myocardium. Advances in anatomy, embryology, and cell biology. Springer, Berlin, New York.

Mayr, M. and Quatember, B. 2007. Imaging and mesh generation issues in patient-specific simulation studies of coronary hemodynamics. In *MODSIM 2007 Conference*, Christchurch, New Zealand.

Meier, B. 2004. Interventional cardiology an atlas of investigation and therapy. Clinical Publishing, Oxford.

Ottesen, J. T. and Danielsen, M. 2000. Mathematical modelling in medicine. Studies in health technology and informatics, v. 71. IOS Press. Ohmsha, Amsterdam. Washington, DC Tokyo.

Quatember, B., Mayr, M. and Mühlthaler, H. 2005. Patient-specific simulation studies of the coronary hemodynamics in a grid environment: Methods imaging and mesh generation issues. In Spitaleri, R. M. editor, *MASCOT05*, 91-100, Lecce.

Quatember, B., Mayr, M. and Mühlthaler, H. 2006. Clinical usefulness of a computational grid for diagnosis and planning therapy of coronary artery disease. In Volkert, J., Fahringer, T., Kranzlmüller, D., and Schreiner, W. editors, *1st Austrian Grid Symposium*, **volume 210**, 75-89, Schloss Hagenberg, Austria. Oesterreichische Computer Gesellschaft (books@ocg.at).

Quatember, B. and Mühlthaler, H. 2003. Generation of cfd meshes from biplane angiograms: an example of image-based mesh generation and simulation. *Applied Numerical Mathematics*, **46(3-4)**, 379-97.

Rougee, A., Picard, C., Saint-Felix, D., Trousset, Y., Moll, T., and Amiel, M. 1994. Three-dimensional coronary arteriography. *International Journal of Cardiac Imaging*, **10(1)**, 67-70.

Singh, V., Xu, J., Hoffmann, K. R., Xu, G., Chen, Z., and Gopal, A. 2006. Towards a theory of a solution space for the biplane imaging geometry problem. *Medical Physics*, **33(10)**, 3647-65.

Soper, N. J., Swanström, L. L. and Eubanks, S. 2005. Mastery of endoscopic and laparoscopic surgery. Lippincott Williams & Wilkins, Philadelphia ; London, 2nd edition.

Trahair, R. C. S. 2002. All about heart bypass surgery. Oxford University Press, South Melbourne, Vic., Oxford.

Zipes, D. P. and Braunwald, E. 2005. Braunwald's heart disease a textbook of cardiovascular medicine. W.B. Saunders, Philadelphia, Pa., 7th ed edition.