On the use of computational models for the quantitative assessment of surgery in congenital heart disease

Konjenital kalp hastalığı cerrahisinin nicelik değerlendirilmesinde bilişimsel modellerin kullanımı

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ABSTRACT

The surgical repair of congenital heart disease often involves significant modifications to the circulatory tree. Resections, reconstructions, graft insertions and the deployment of implants and biomedical devices have an impact on local and systemic haemodynamics, which may be difficult to foresee or to assess quantitatively by clinical investigation alone.

Mathematical models can be employed to visualise, estimate or predict events and physical quantities that are difficult to observe or measure, and can be successfully applied to the study of the pre- and post-operative physiology of cardiovascular malformations.

This paper analyses the potentialities of computation fluid dynamics in this respect, outlining the method, its requirements and its limitations. Examples are given of lumped parameter models, axi-symmetric models, three-dimensional models, fluid-structure interaction simulations and multiscale computing applied to total cavo-pulmonary connection, aortic coarctation and aortic arch reconstruction. *(Anadolu Kardiyol Derg 2005; 5: 202-9)*

Key words: Mathematical models; congenital heart disease; coarctation of aorta; total cavo-pulmonary connection; computational fluid dynamics.

ÖZET

Kojenital kalp hastalıklarının cerrahi tamiri dolaşım ağacının birçok modifikasyonunu içerir. Rezeksiyonlar, greft takılması, implant ve biyomedikal araçların yerleştirilmesi lokal ve sistemik hemodinamiği etkiler. Bu da klinik takibi kantitatif olarak öngörmeyi ve değerlendirmeyi zorlaştırabilir.

Matematik modeller; gözleminin ve ölçmenin çok zor olduğu olayların ve fiziksel değerlerin görüntülenmesinde, tahmin edilmesinde ve öngörülmesinde kullanılabilir. Matematik modeller yine kardiyovasküler malformasyonların fizyolojisinin ameliyat öncesi ve ameliyat sonrası çalışılmasında başarıyla uygulanan bir yöntem olmuştur.

Bu makale bilgisayarlı akışkan dinamiklerinin potansiyellerini, metodolojisini, gerekliliklerini ve sınırlarını analiz etmektedir. Örnek olarak verilmiş çeşitli parametre modelleri, aks-simetrik modeller, üç boyutlu modeller, akışkan-yapısal ilişki simülasyonları ve çok ölçekli bilgisayar modelleri, total kava-pulmoner bağlantı, aort koarktasyonu ve aortik ark rekonstruksiyonuna uygulanmıştır. *(Anadolu Kardiyol Derg 2005; 5: 202-9)*

Anahtar kelimeler: Matematik modeller; konjenital kalp hastalığı; aort koarktasyonu; total kavo-pulmoner bağlantı; bilgisayarlı akışkan dinamikleri

Background to Computational Fluid Dynamics

Mathematical Modelling

Mathematical modelling is the general name given to methodologies that utilise mathematical equations as a way of describing and studying physical phenomena. Mathematical models can be employed to visualise, estimate or predict events and physical quantities that are difficult to observe or measure, and can help investigate and understand the complexity of nature.

In the history of Applied Mathematics many different approaches to modelling have been attempted. Over the centuries this effort has yielded a number of validated and successful descriptions of our physical world at diverse scales and levels of accuracy. Some of these descriptions, although very sensible and reliable, are governed by extremely complex equations, for which an exact solution can be derived at best only in very particular and simple cases. Such 'simple cases' are often characterised by high symmetry, homogeneity of physical properties and geometrical regularity; low levels of compartmentalisation and

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scarce interaction with external entities. Obviously, natural occurrences possessing more than one or two of these qualities are extremely rare and, generally speaking, tend to inspire very limited interest to any practical purpose. Unfortunately this implies that, in the vast majority of our scientific endeavours, we are faced with problems of high complexity that cannot be solved in traditional ways.

Choice of equations and problem set-up

Devising a mathematical model is therefore a two-stage process and finding a solution to it involves a separate extra step. Let us now consider the first two steps: choosing the governing equations and particularising the current problem.

In principle, the initial choice of equations is quite a straightforward issue. If we are going to solve a problem involving, say, currents and voltages, the equations will have to be the Electromagnetism ones, for fluids we shall use Hydraulics, for deformable solids Continuum Mechanics, and so on. Picking the most general form of the equations may not necessarily be the wisest tactic, however. General equations tend to be quite complex and may contain terms that account for physical quantities and phenomena that are hardly implicated in the particular problem of our current interest and could therefore be neglected. Using these would make the model more difficult to solve, or in some cases impossible.

In order to make a decision we have to start dealing with the second step as well: the problem. Mathematically this implies setting values for all of the constants in the equations and defining geometry, and boundary and initial conditions.

The constants are generally related to properties of the materials involved, to some reference value of physical quantities, or to some reference geometrical dimension. Purely considering these constants, some conclusions can be drawn on what terms may be left out of the governing equations.

Geometry obviously plays a major role in describing a problem, as objects of different shapes tend to move and deform in different ways.

The initial conditions are needed when the governing equations contain time derivatives, and they set the state of the system at the beginning of the period of time for which the model has to be solved.

The boundary conditions reflect the interaction of the modelled system with its surroundings that, although not modelled, interact with it across its boundaries (e.g. by compressing it, heating it, filling it with some substance, holding it in a certain position, etc).

When the problem is defined, the overall complexity of the model can be estimated and, if deemed excessive, the model has to be edited and simplified, possibly neglecting aspects of the problem that one would initially have liked to include. In this way, a final compromise should be reached between the investigator's need for accuracy and the possibility of actually solving the model, which, at present, mainly lies in the availability of computer power, as explained next.

Computational fluid dynamics

When the equations governing a certain phenomenon are mathematically complicated, and are applied to a complex problem, only an approximate solution can be generated for the model. This is done utilising numerical calculus strategies. These exploit the potentialities made available by constantly developing computer technology.

The solution schemes vary greatly with different applications, but they all share some basic principles. Methodologies of this kind, used in the branches of engineering that deal with moving fluids, can be grouped under the name of computational fluid dynamics (CFD).

After being successfully employed in numerous fields of traditional engineering, CFD also started to develop as an important tool in connection with Bioengineering, particularly in the haemodynamics applications. Nowadays, under the name CFD one should also include fluid-structure interaction (FSI) simulations, in which not only the equations governing the fluid are solved, but also those that describe deformable solids interacting with the fluid.

The numerical methods used in CFD simulations are based on spatial and temporal discretisation. Accordingly, a grid, which is generally referred to as the computational mesh, is used to discretise the volume-of-interest, i.e. to divide it into elements. These elements are defined with reference to the nodes of the mesh. The physical and structural properties of the substances represented (in our case blood and vessel walls) are assigned to the corresponding sets of elements in this mesh. Boundary and initial conditions that specify the particular problem to be solved are assigned at the nodes. This special discretisation reduces field problems (that have an infinite number of unknowns) to problems with a finite number of degrees of freedom, but entails the approximation that the solution will be available only at a discrete number of points in the volume. Computational fluid dynamics methods also include discretisations in time, that limit the number of instants at which the solution is known. The density or refinement of the space and time discretisations is key in determining the level of accuracy. High refinement is, however, related to high simulation times and, in the extreme, to the impossibility for the machine to provide a solution. Node densities that change across the geometry can generally be assigned in order to achieve greater accuracy in the portions of the volume that are most interesting to monitor, or in which the solution has particularly steep gradients. Another factor that carries along a trade-off between computer resources and solution accuracy is the choice of the model scale. For many problems it is possible to conceive models in 0D, 1D, 2D, 2.5D (axi-symmetric) and 3D. The higher the dimensionality, the higher the cost. Also, the reliability of this method depends on the type of problem. In particular, issues may arise when the boundary conditions are based on too much guesswork, or the geometry is too simplified, or the material properties are not accurately represented. The level of assumptions that is acceptable must be decided on the basis of the scientific knowledge of the relative importance of different aspects of the problem, but this knowledge as a prerequisite is sometimes not available. In addition to this, errors can derive from the fact that the available computer power may be too small for the high numerical accuracy expected. Notwithstanding these drawbacks, CFD reliability is currently greater for laminar flows than for turbulent ones; for single-phase flows than for multiphase flows; for chemically inert than for chemically reactive materials; for single chemical reactions than for multiple ones; for simple fluids than for complex mixtures.

Computational Fluid Dynamics and Congenital Heart Disease

Research questions

The important role played by haemodynamics in determining a patient's state in the context of pathological or post-surgical circulatory conditions has long been recognised. Anomalous blood vessel connections, stenoses, aneurysms, partial or total occlusions, compromised vessel wall properties, can all severely impair the normal blood flow patterns, flow repartition and pressure and energy drops. More subtly, endothelial physiology can also be affected as a result of disturbed blood motion and the vessel wall functionalities may be prejudiced.

In light of this, it is fundamental to be able to assess qualitatively and quantitatively the amount of disturbance caused by disease primarily, and also by the modifications introduced at the time of surgery or interventional cardiology through resections, reconstructions, graft insertion and the deployment of implants and biomedical devices. A quantitative analysis of haemodynamics could lead to a different kind of classification of disease severity and of surgical efficacy.

Although the value of clinical investigation in this respect is remarkable, there are instances in which this approach cannot suffice, given the insurmountable limits posed by ethics and by the state of current measurement techniques. Especially when faced with very complex diseases, it is very difficult for a researcher to be able to collect reliable measurements for all the variables of interest in all the implicated districts. In fact, this task can often become impossible even in relatively simple settings when the accuracy and resolution requirements are high, mainly due to the characteristics of the available machinery or the long acquisition times.

When clinical tests fail to describe circulatory variables in an acceptable way for the needs of a certain research, or when it is impossible to simulate particular physiological or anatomical conditions; when abstraction from subject individuality is required or a validation of uncertain clinical results is sought, computational modelling can be an alternative path which can help shed light on obscure areas in the physiology and surgery of blood circulation.

A good idea of the possible uses of these methodologies in tackling CHD-related issues can be acquired from the numerous papers published on the subject (1-13).

Requirements and limitations of the computational approach

As reported in the Background to Computational Fluid Dynamics, the formulation of mathematical models is based on the use of certain governing equations and the assignment of appropriate conditions that describe univocally the research question. In the case of blood circulation, the elements that play a role in the problem definition greatly depend on the scale of the model required: at nano-level electrical charges, molecular structure and substrate characteristics; at the micro-level cellular and macro-molecular mechanical properties. Considering larger scales, at tissue level (and occasionally organ level), the tissue global mechano-physical properties become important, as well as the geometry, the mutual position of different tissues and the interactions with neighbouring anatomical structures. Finally, at body level, very often only averaged properties for relatively large structures, roughly the size of major blood vessels, organs or circulatory districts can be accounted for; geometrical factors often have to be neglected altogether, or greatly approximated.

In congenital heart disease (CHD), in both pre- and post-surgical configurations, the greatest interest probably lies in the development of tissue-organ-body models. At these scales blood vessel segments, circulatory districts or the whole blood circulation can be modelled, naturally with different levels of detail. Hence the need for specific conditions for these types of problems.

For the tissue-organ level, axi-symmetric and 3D models are often the best choice. Physical parameters, such as the blood density and its viscous behaviour (be it Newtonian or non-Newtonian), and the vessel wall density and its elastic or viscoelastic characteristics, must be chosen. When modelling CHD repairs, analogous characteristics are also required for the graft materials employed. All these parameters can be determined by physical examination, mechanical testing, or can often be derived from the published literature. Moreover, boundary and initial conditions have to be selected. For this type of problem, boundary conditions are generally in the form of velocity profiles on the inlets, and pressures on the outlets; or, alternatively, pressure on both inlets and outlets. Furthermore, if apart from the blood motion, the interaction between the vessel wall and the fluid is also modelled (FSI), then displacement and/or velocity conditions may be necessary to limit the structure deformation and roto-translation. Obviously, all these conditions must be determined for the specific problem, mainly by clinical measurements, which in some occasions can be problematic, especially if there are non-invasiveness constraints. The use of magnetic resonance imaging (MRI) has recently been recognised as one of the best methods for acquiring velocity data and realistic geometrical (anatomical) information at the same time. For this purpose Doppler ultrasound may also be useful in certain settings. As for the pressure waveform acquisition, catheterisation is frequently the only option, even though alternative non-invasive techniques such as applanation tonometry may be considered in particular cases. The difficulty of acquiring reliable boundary and initial conditions is one of the limitations of computational methodologies, together with the aforementioned dependence on computer power availability. On the other hand, the use of CFD definitely cuts down on the number and extent of measurements required to characterise a certain haemodynamic state because, apart from the boundary and initial conditions, all the other variables of interest can be calculated. An attempt to free CFD modelling of the limitations imposed by boundary condition acquisition is the use of multiscale computing, in which parts of the system beyond the boundaries of the tissue-organ model are also accounted for, generally by a body scale representation.

Body scale models are useful not only in the context of multiscale methods but also as full models in their own right, when the research object corresponds to some very extended portion of the circulatory tree. These models are generally based on the definition of equations dependent on time alone (0D) or, at most, on time and a longitudinal dimension along the blood circuit (1D). The parameters in these equations are global quantities describing the viscous resistance encountered by blood in its movement through the compartments of circuit; the inertia that, at various locations, opposes variations in blood speed; the compliances of the vessel walls, and so on. Such a model may or may not require any boundary conditions, depending on whether it is an open or a closed circuit. The problem here lies in the estimation of all of the parameters needed, which is ultimately based on clinical measurements and their mathematical elaboration. Computation time is generally not an issue in this type of model, and the main drawback is the limited detail provided, although it may well be sufficient for several applications.

Examples of Application of Computational Fluid Dynamics to Congenital Heart Disease

Lumped parameter model for the study of total cavo-pulmonary connection

Total cavo-pulmonary connection (TCPC) is an important and complex surgical intervention that aims to treat a wide class of congenital diseases characterised by single ventricle physiology. The operation strongly modifies the original setting of the circulatory tree: the systemic and pulmonary circuits, which in the presence of a single functional ventricle are in parallel, are connected in series. Such a change has side effects on various cardiovascular variables throughout the circuit and on the post-surgical physiology as a whole. A mathematical model of the short/mid term post-operative paediatric circulation helps to analyse and make decisions about the use of such a therapeutic strategy.

This is a body-scale problem because the whole blood circulation is involved. For this reason, 0D models were chosen. These are also known as lumped parameter models (LPM).

A lumped parameter model of the healthy paediatric blood circulation was developed, based on a full range of characteristic constants that describe the behaviour of heart, pulmonary and systemic circulations with particular regard to the venous return. This model was compared with another lumped parameter model comprising all major aspects of the TCPC post-operative anatomy and physiology. Such aspects include a model of the univentricular heart, of the actual anastomosis and of the chronic adaptation that occurs following the intervention. The models obtained were tested against clinical measurements found in the literature. The model schemes are shown in Figure 1.

These models give very accurate predictions of velocity/flow and pressure tracings, and absolute values of circulatory variables throughout the system. As an example, Figure 2

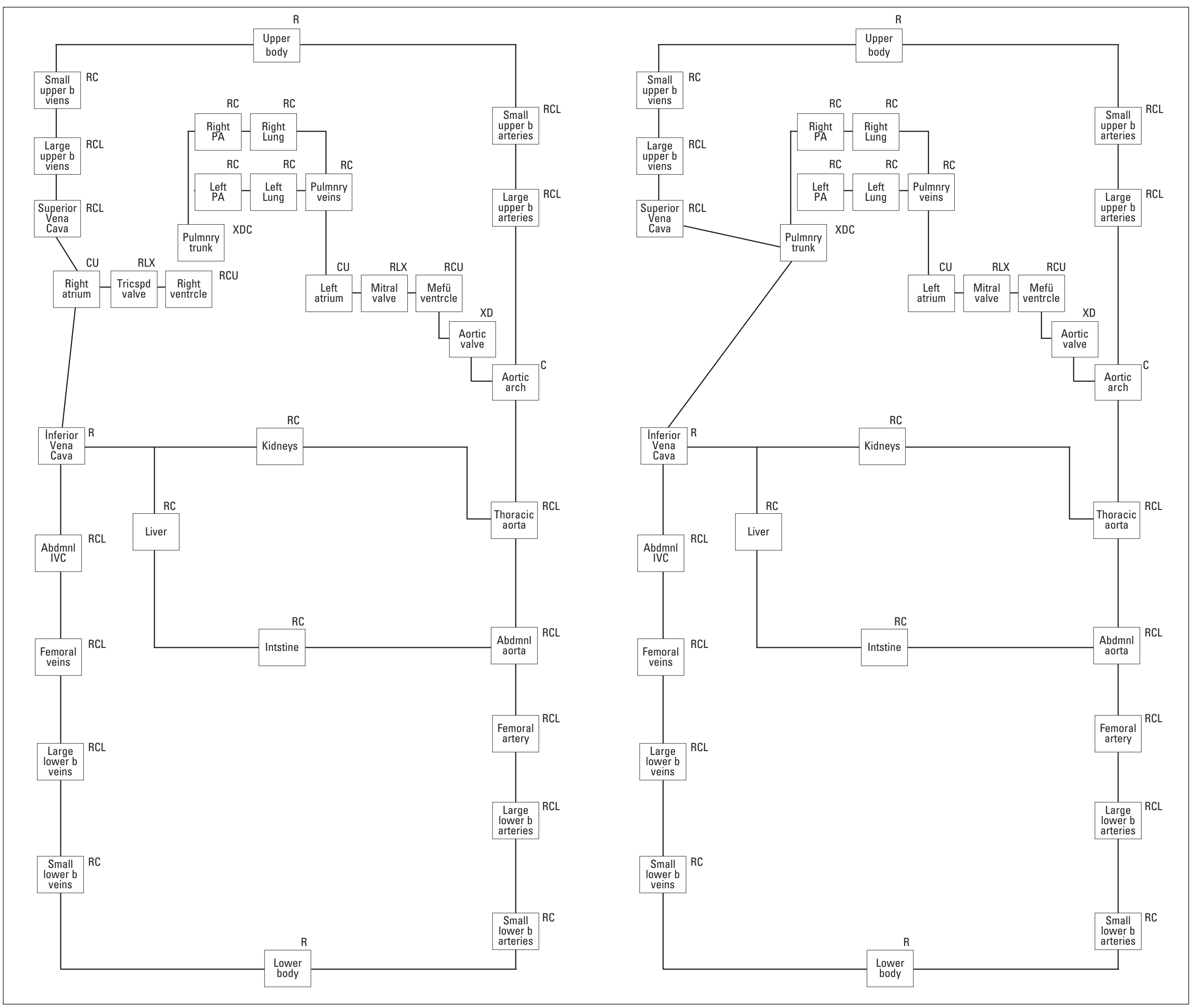

Figure 1. Schemes of lumped parameter models for the healthy paediatric circulation (left) and the total cavo-pulmonary connection arrangement (right). Letters near each block represent parameters built in the block. R: hydraulic resistance; C: blood vessel compliance; L: blood inertance; D: localised energy loss; X: valve function; U: pressure generator.

shows a comparison with clinical measurements derived from the literature for the velocity in the hepatic vein.

Simulations of post-operative scenarios can deal with the effects of a paralysed diaphragm (Fig. 3), of an increase in pulmonary resistance, of a uni- or bilateral pulmonary artery stenosis or of exercise, for instance. Details of this study can be found in the literature (14,15).

Multiscale models for the study of the interaction of aortic coarctation and its repairs with the blood circulation.

Coarctation of the aorta (CoA) is a congenital narrowing of the upper descending aorta, which is sufficiently severe to create a pressure gradient across the area. There is an open debate about the causes that lead to re-coarctation, hypertension and/or aneurysm formation after CoA repair in a significant number of cases. It is important to try and assess the treatment outcomes quantitatively, and to ascertain the indications for the different surgical techniques.

Axi-symmetrical models for a healthy subject, for CoA, for an end-to-end repair (E/E) and for a Gore-tex graft interposition repair (GGI) were created. These include compliant walls. Boundary conditions on the axi-symmetric models are in the form of inlet and outlet pressures and are calculated by a lumped-parameter net, whose inlet and outlet flows are the solutions of the axi-symmetric models according to a multiscale approach. The lumped parameter net comprises variable degrees of collateral vessel development (Fig.4).

Some of the possible results for this type of model are: pressure contours, velocity field, vortex permanence, energy losses, shear stresses, stresses in the wall, etc, for the axi-symmetric models; pressure and flow waveforms for the lumped parameter net. In this way comparisons between different types of repair, pre-operative conditions and normality can be made. The role

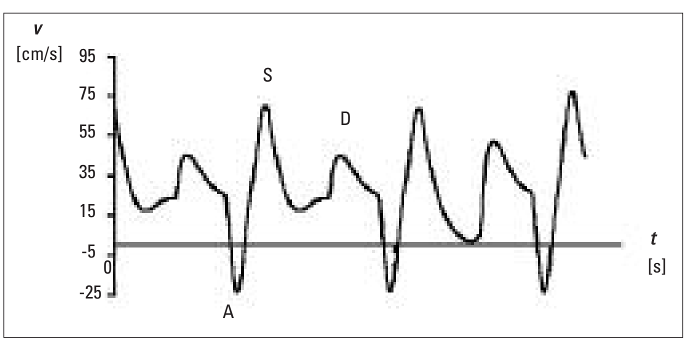

Figure 2. Calculated paediatric superior vena cava blood velocity (compare e.g. with Doppler recording by Salim et al.(16)

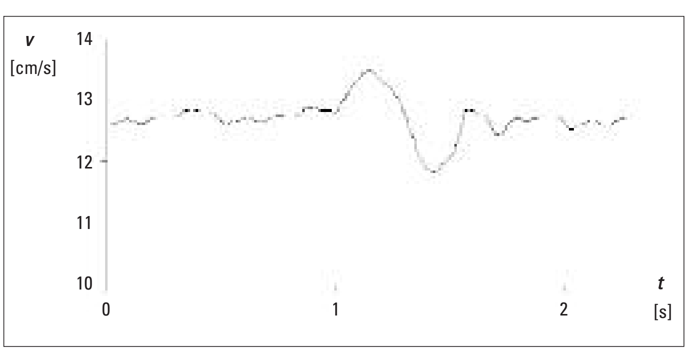

Figure 3. Calculated superior vena cava blood velocity plot of total cavo-pulmonary connection patient with paralyzed diaphragm
SVC:superior vena cava, V: velocity, t-time

played by the abundance of collateral flow can also be estimated. An example of calculated velocity field is given in Figure 5. Axi-symmetric models are useful in this case for concentrating the attention on the influence of different tissue properties, rather than patient-specific anatomy (see 3D models below). The use of a body-scale 0D net makes it possible to study the influence of localised disturbances on the whole system. Further details of this study can be found in the literature (17).

Rigid wall - steady flow models of the total cavo-pulmonary anastomosis

Models of the anastomosis region in total cavo-pulmonary connection were developed (Fig. 6) in order to compare the local fluid dynamics of the lateral tunnel (LT), intra-atrial or intracardiac conduit (ICC) and extra-cardiac conduit (ECC), including the infuence of the infra-diaphragmatic venous vessels (hepatic veins). Different anastomosis angles were also created and the use of different conduit sizes was modelled.

In order to perform realistic simulations, the three-dimensional models were completely constructed using patient-derived information: three-dimensional geometry based on angiography pictures from various angles; local inlet velocity flows from Doppler recordings; outlet pressure boundary conditions from in vivo catheter measurements.

Inlet flow boundary conditions were defined at the two HV branches, sub-hepatic IVC, and SVC. Outlet pressure boundary conditions were defined at the four PA branches.

For these models it was assumed that vessel walls are rigid and that the flow is non-pulsatile. The rigid wall assumption was forced by the complexity of the geometry (branchings) and by the technology available at the time, but it is acceptable given the low pressure values registered in this region. Non-pulsatility is an acceptable assumption in this venous compartment, especially because the right atrium is disconnected during TCPC.

Computational solutions calculated the percent hydraulic power dissipation and left-to-right pulmonary arterial flow distribution in different configurations. As a result, extracardiac conduit with left pulmonary artery anastomosis appeared to have the lowest energy loss, especially with tubes of larger diameter. Conversely, serial dilation of the lateral tunnel pathway showed a small incremental worsening of energy loss. Maximizing energy conservation in a low-energy flow domain, such as the Fontan circulation, can be significant to its fluid dynamic performance. Although this computational model cannot predict postoperative failure or functional outcome, it helped confirm the importance of local geometry of the surgically created pathway in the total cavo-pulmonary connection.

Models of this sort can be used to predict local energy losses, flow repartition and pressure drops. More details on these models can be found in the literature (18).

MRI-derived compliant wall models of reconstructed aortic arches with active afterload

Surgically reconstructed configurations of the aortic arch and proximal descending aorta are very complex haemodynamic and structural systems, in which the blood flow interacts with tissues of different mechanical properties and moves inside a three-dimensional and asymmetric anatomy, itself subject to movement and deformation.

The possibility of taking into consideration all these different aspects is potentially provided by the FSI approach. Difficulties arising in the formulation of an FSI model of such complexity as the one described are mainly concerned with the identification of appropriate boundary conditions, and generally with the commercial availability of limited computing power. These issues lead to the need to accept a certain number of approximations at the current stage (e.g. imprecise tissue characterisation), but do not prevent us from obtaining interesting results.

Such simulations can provide a means to compare the alternative use of different surgical techniques for the reconstruction of the aortic arch and proximal descending aorta. Using the same anatomy for all models allows us to set aside all diversities that might derive from specific individual anatomies (Fig.7). Therefore, the study can be devised as a comparison between possible outcomes of different surgical corrections on the same patient. The anatomical model in our case was derived from an MRI dataset obtained from a healthy 40kg sow of Danish breed. A health control, the end-to-end repair (E/E), Gore-tex graft interposition (GGI), and Gore-tex patch aortoplasty (GPGA) were modelled and compared.

The use of an open lumped parameter net (LPM) for the imposition of outlet conditions on the 3D models (3DM) provides the system with an afterload stage able to react in an active way to the variations occurring from one type of model to the next. It also allowed us to look into the influence of localised changes on the haemodynamic conditions of peripheral districts. The inlet boundary conditions are assigned in the form of an inlet flow derived from MRI measurements.

The full results of these simulations, in terms of stress distributions, flow fields, energy losses, pressure distributions, etc, will be published shortly. Briefly, this study suggests that stress concentration occurs in the suture areas in all set-ups, especially along the sides of the aortic wall (rather than on the inside or outside of the curvature). Overall wall shear stress distribution does not vary much, although slightly higher values are registered for GGI, GPGA and E/E respectively. The velocity field

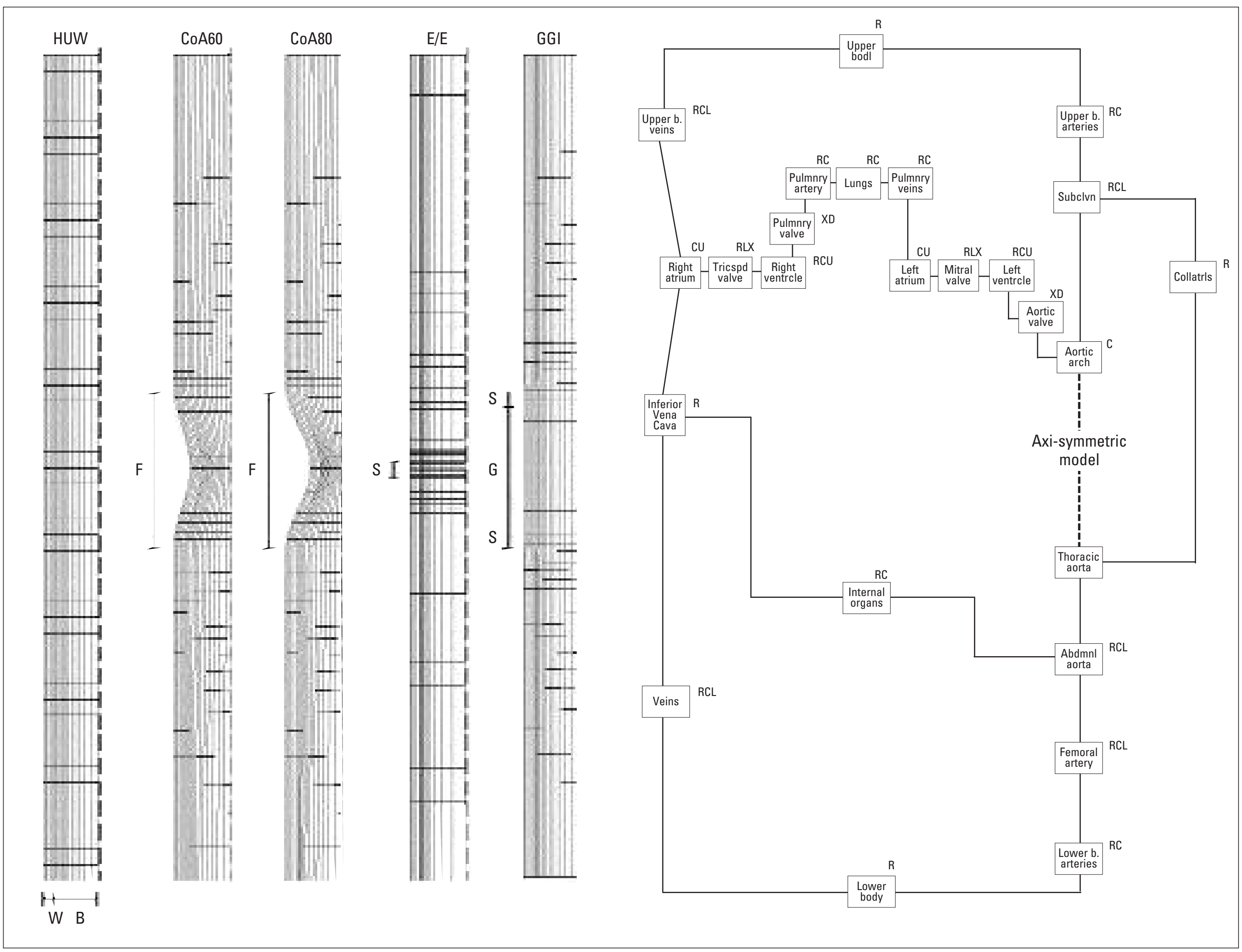

Figure 4. Axi-symmetric models and coupling with the lumped parameter net. Letters near each block represent parameters built in the block. R: hydraulic resistance; C: blood vessel compliance; L: blood inertance; D: localised energy loss; X: valve function; U: pressure generator.

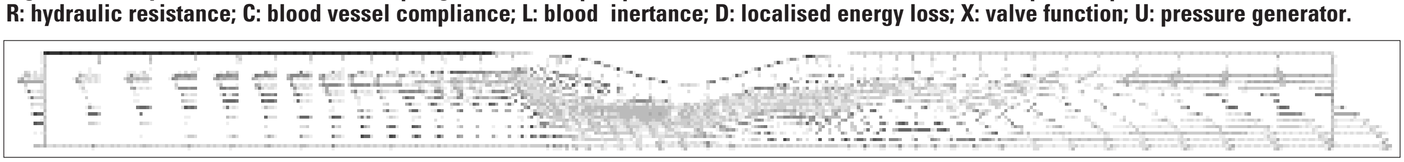

Figure 5. Flow reversal phase of the cardiac cycle with a 60% stenosis

appears to be most affected by GPGA. In general, however, geometry seems to be the main drive of any haemodynamic alteration. Different wall material properties therefore appear to be significant in defining haemodynamics, particularly when they affect geometry by changing tissue deformation patterns.

Acknowledgements

Research at the Institute of Child Health and Great Ormond Street Hospital for Children NHS Trust benefits from Research and Development funding received from the NHS Executive. Mr Pittaccio is supported by the British Heart Foundation.

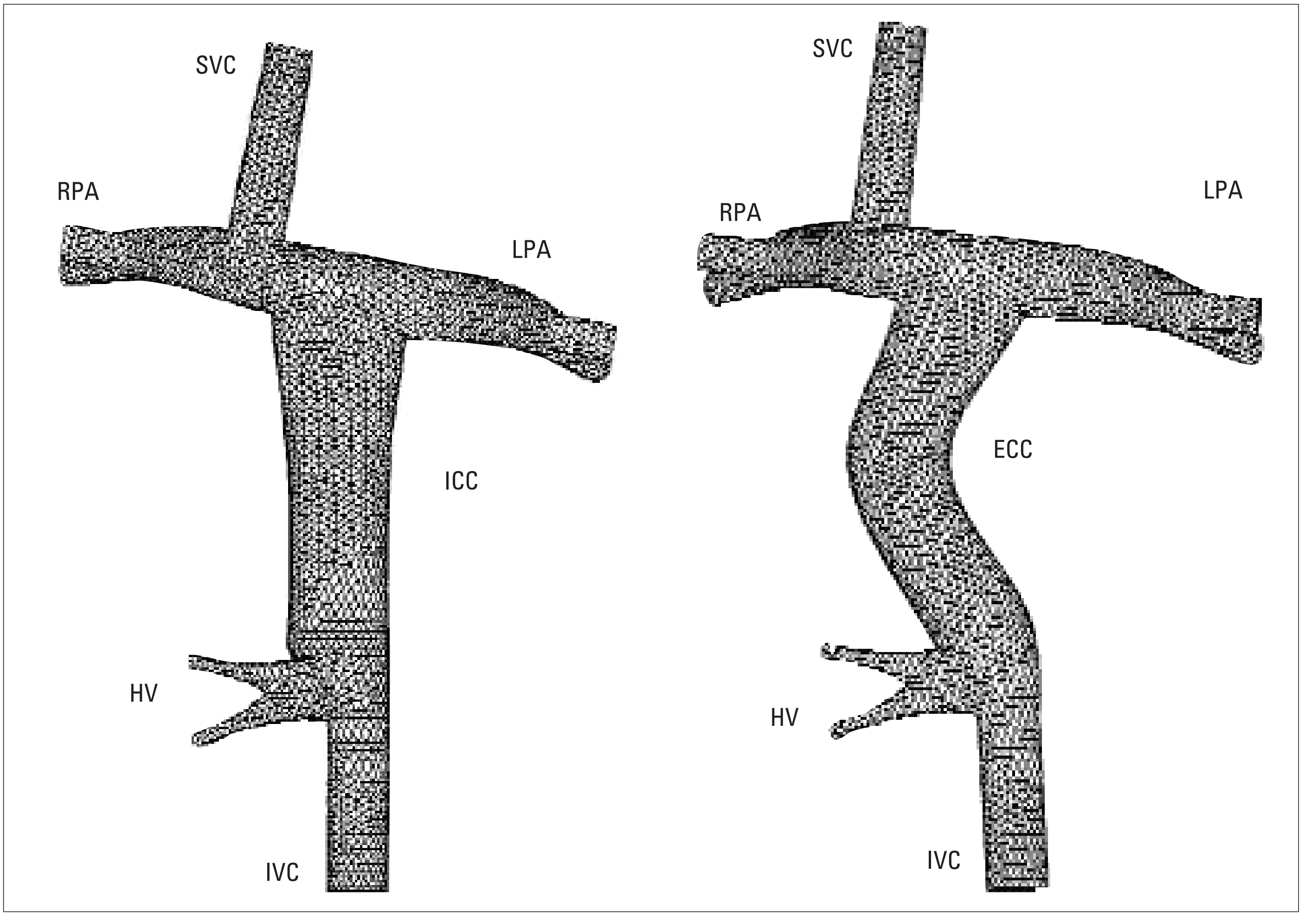

Figure 6. Models of the intracardiac conduit and one type of extracardiac conduit in total cavo-pulmonary connection
ECC: external common carotis artery, HV: hepatic vein, ICC: internal common carotis artery, IVC: inferior vena cava, LPA: left pulmonary artery, RPA: right pulmonary artery, SVC:superior vena cava

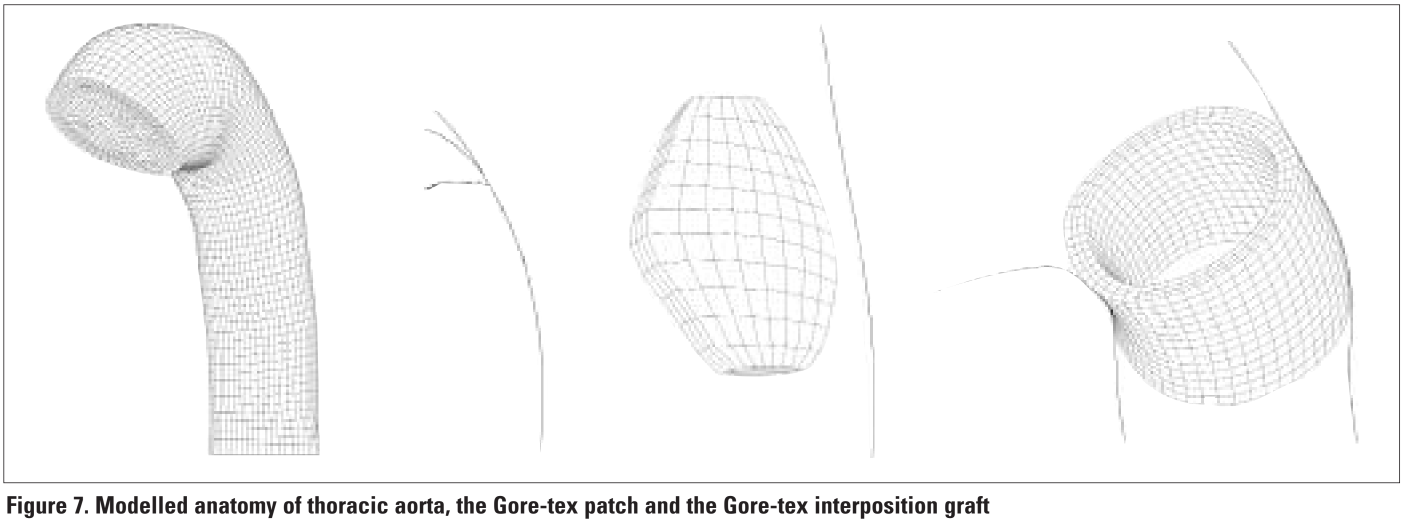

Figure 7. Modelled anatomy of thoracic aorta, the Gore-tex patch and the Gore-tex interposition graft

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