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## Mathematics and Cardiovascular Interventions



### Role of the Finite Element Modeling in Clinical Decision Making

Nowadays, mathematical and numerical models are becoming increasingly important in cardiovascular medicine. In mathematics, the finite element method (FEM) is a numerical technique used to analyze complex structures. This method subdivided a whole problem domain into simpler parts, called finite elements (FEs). Although mathematics might seem of little utility in clinical practice, several clinical reports have shown that altered flow conditions, such as flow reversal, shear stress, and flow separation, are fundamental factors in the development of arterial diseases. In this setting, the possibility to understand and predict hemodynamic alterations and long-term adaptation of the cardiovascular system, before and after surgical or interventional procedures, could be a very useful tool for surgeons and cardiologists, also for modifying their therapeutic strategies. In cardiovascular modeling, the geometric proprieties of heart and vessels are generally derived from magnetic resonance imaging, computed tomography, or angiography and then converted into the FE geometry using special commercial software. On the other hand, the material physics properties are derived from existing biomechanical studies of the tissue involved. Conventionally, computer simulation of solid and fluid structure interactions is based on the Arbitrary Lagrangian-Eulerian method. Different cardiovascular diseases have been studied via this process. Cupps et al. (1) examined the regional left ventricle wall stress in aortic regurgitation (AR) and normal systolic function, showing that it was significantly higher compared with patients with normal aortic valves. In a similar way, AR has been studied, analyzing both leaflet stress and strain (2). Computational fluid dynamic analysis (CFD) was also applied to assess the residual stress produced by ventricular volume reduction surgery, demonstrating the small post-operative effect on left ventricular function. Instead, Toeg et al. (3) focused their analysis, using the FEM, on the "ideal" biomaterial for aortic valve repair (AVr), considering that in past years, AVr has become an

attractive alternative to aortic valve replacement. Similarly, Qiao et al. (4) assessed the reason of neo-aortic valve insufficiency after Ross procedure. The problem of AR due to a congenitally undersized leaflet was studied by some cardiac surgeons, who have shown that aortic root reduction can improve valve closure and eliminate regurgitation, but the result is strongly connected to both the shape and size of the resected area. Ascending thoracic aortic aneurysms were analyzed through CFD analysis which investigated aneurysm wall stress, identifying the site most prone to rupture. The mitral valve was studied by the FEM, in both normal conditions (analyzing its deformation under physiological loading conditions) and in pathological conditions. Recently, some researchers evaluated the possibility of assessing optimal mitral valve repair in a small cohort of patients using the FEM, opening the way to patient-specific optimization of surgical treatment through cardiovascular modeling. Important findings have also emerged regarding cavopulmonary shunts: the classic Norwood central shunt and the modified Blalock-Taussig procedure have been described and compared. Moreover, application of mathematical computational methods have been used as the basis for coronary angiography/computed tomography-based prediction of fractional flow reserve relative to the coronary artery lesion and for predicting coronary bifurcation adaptation to different stenting techniques (5). Multiple applications of the FEM in cardiac surgery and interventional cardiology are in the pipeline. In the near future, the FEM will be a modeling tool that will allow realization of a patient-specific approach.

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## Patient-Specific Computer Modeling to Predict Aortic Regurgitation After Transcatheter Aortic Valve Replacement

Outcome of transcatheter aortic valve replacement (TAVR) depends on a combination of patient-, procedure-, and operator-related variables. Specific device-host-related interactions may also be involved and may result in, for instance, incomplete and/or nonuniform frame expansion that in turn may lead to aortic regurgitation (AR) (1). Due to the large variability of the aortic root anatomy, the occurrence and severity of AR is hard to predict, indicating the need of tools that help the physician to select the type and size of valve that best fits the individual patient in addition to the optimal landing zone. Computer simulation of a TAVR procedure that is based upon the integration of the patient-specific anatomy, the physical and (bio)mechanical properties of the valve, and recipient anatomy may serve this goal (2). We herein describe such a model for AR prediction that was validated in a series of 60 patients who underwent TAVR with the Medtronic CoreValve Revalving System (MCS) (Medtronic, Dublin, Ireland).

For that purpose, pre-operative multislice computed tomography (MSCT) was used to generate patient-specific 3-dimensional models of the native aortic root using image segmentation techniques (Mimics v17.0, Materialise, Leuven, Belgium). Subsequently, implantation of virtual CoreValve models in these aortic root models was retrospectively simulated using finite-element computer modelling (Abaqus v6.12, Dassault Systèmes, Paris, France), resulting in a prediction of frame deformation and native leaflet displacement. Details of this method, as well as the validation of the predicted frame deformation, have been described before (3). In each computer-simulated implantation, all steps

of the clinical implantation were respected, consisting of pre-dilation, valve size selection, depth of implantation, and post-dilation if applied. The depth of implantation was matched with the actual depth of implantation derived from contrast angiography performed immediately after TAVR.

The blood flow domain including the paravalvular leakage channels (if any) was then derived from the predicted frame and aortic root deformation, and computational fluid dynamics (OpenFOAM v2.1.1, OpenCFD, Bracknell, United Kingdom) was used to model blood flow during diastole with the aim of assessing the severity of aortic regurgitation after TAVR. For this purpose, a fixed pressure difference of 32 mm Hg was imposed from the ascending aorta to the left ventricle. The actual pressure difference post-TAVR was intentionally not used as the aim is to validate a model predicting AR based on pre-operative MSCT only (i.e., when the pressure post-TAVR is unknown). The value of 32 mm Hg is an average obtained from a large group of patients. The resulting flow, expressed in ml/s, was compared with the clinically assessed AR. The modelling of AR is illustrated in **Figure 1** showing 2 patients with different severities of AR.

Contrast angiography and Doppler echocardiography were used for the assessment of AR. Analogous to the CHOICE (A Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis) study, AR severity by contrast angiography was defined by visual estimation of the contrast density in the left ventricle using the Sellers classification (0 = none/trace, 1 = mild, 2 = moderate, 3 = severe; the latter comprised grades 3 and 4 according to Sellers) (4). Two observers independently from one another scored the angiograms. In case of discrepancies, consensus was reached by consulting a senior cardiologist. The intraobserver and interobserver variability for the assessment of AR post-TAVR according to the Sellers classification were  $\kappa$  0.70 and 0.78, respectively. Doppler echocardiography was performed before discharge. AR severity was defined by the circumferential extent of the Doppler signal at the inflow of the MCS frame in the parasternal short-axis view (VARC-2 [Valve Academic Research Consortium-2]) (5). Echocardiography was available in 56 of the 60 patients. Distinction was made between none (grade 0), mild (<10%, grade 1), moderate (10% to 29%, grade 2), and severe ( $\geq$ 30%, grade 3) AR. Physicians performing TAVR and engineers performing the simulations were blinded to one another's results.

Moderate-severe AR (Sellers AR  $\geq$ 2) post-TAVR was seen in 15 patients (25%) by angiography. The