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Data Paper

Circulatory Modelling as a Clinical Decision Support and an Educational Tool

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ABSTRACT

Circulatory models can be used in support of clinical decision making. Based on this assumption, we developed a modelling platform composed of a family of circulatory models based on a polymorphic structure. The models of the family permit the reconstruction of patient's status in various pathophysiological conditions and can be used in retrospective and prospective ways to formulate hypotheses on the effects of different therapeutic strategies, including the use of mechanical circulatory assistance, mono and bi-ventricular pacing and congenital heart defects. The models can be used for educational purposes, can be controlled remotely and can behave as virtual patients. They can generate data files in Excel format.

Overview

Modelling can be a powerful tool for analysing the complex interactions among the heart, the circulatory system and the therapeutic interventions (drugs, surgery, assist devices), modifying the existing dynamic balance between the heart and the circulatory system.[1-3] The advantages of modelling lie in the possibility of analysing the sensitivity of several circulatory and ventricular variables to the patient's specific therapeutic intervention and, conversely, the effects of selected circulatory and ventricular parameters on the therapeutic intervention performance. In this context, the model can be regarded as a "virtual patient" replicating the conditions of the "real patient." The data produced by the model can be treated as a database containing information on patient's baseline along with the analysis of the effects of different thera-

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peutic interventions. In this sense, the model can support clinical decision making and serve as a tool for prospective and retrospective patient's analysis.

This approach to modelling is based on lumped parameters models (LPM) [4-8] as they have the pre-requisites needed for a daily clinical application: fast response, simplicity of use, reliability and easiness to be modified or re-adapted. Last but not least, thanks to their intrinsic simplicity, it is possible to tune LPMs using routinely acquired clinical data.

Methods

To pursue the aims outlined above, a family of circulatory models was developed. The models of the family are assembled in a modelling platform and share some basic features:

- Lumped parameters structure
- Modular structure
- Polymorphic structure
- Algorithms to adapt the model parameters to the patient's status
- Educational functionalities.

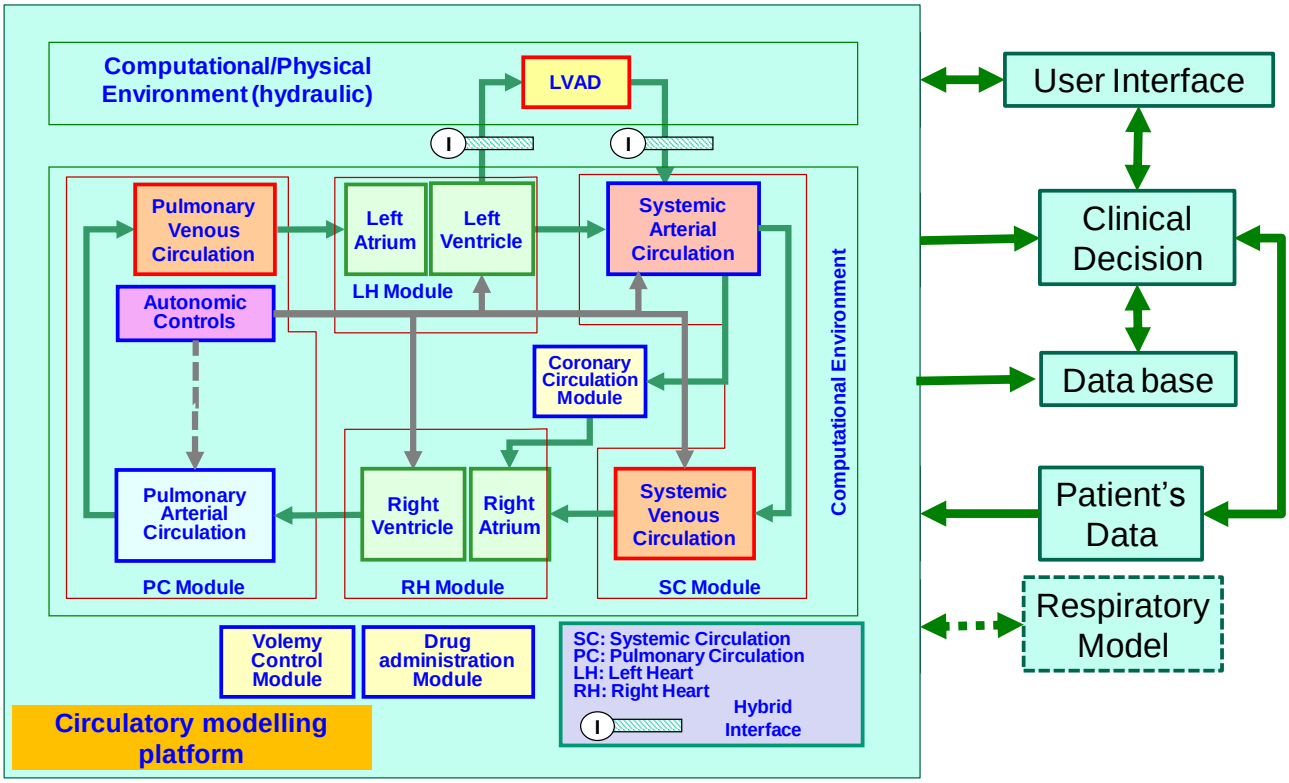

Figure 1: Block diagram of the circulatory modelling platform.

Figure 1 presents the basic structure of the models. Each block presented in the figure contains several modules that can be assembled and used according to specific needs. Among others, the modules sketched in Fig.1 contain a complex of simpler models of systemic and pulmonary circulation,[7-8] models of congenital heart defects[9] and of surgical procedures,[10] interfaces to respiratory models, now under development, models of heart assist devices (LVAD, RVAD, BVAD, IABP, BIV pacing),[11-13] models of autonomic controls (in this moment baroreflex and metabolic controls, the second one under development),[8,14] and interfaces for educational use of the platform.[8]

The polymorphism of the structure has been achieved through implementation of the concept of hybrid modelling,[15-19] in cooperation with the Nałecz Institute of Biocybernetics and Biomedical Engineering of the Polish Academy of Science. In short, hybrid models permit to merge computational and physical models when and if necessary. That is to say, a computational modelling platform with hybrid features can be transformed, if necessary, into a model interfaced, for example, with a mechanical heart assist device,[19] replacing therefore the model of the device with the real device with all the implicit research and educational implications.

The model has been developed for clinical applications and, towards this aim, of fundamental importance is that the model can easily adapt its parameters to a patient's status. This goal is achieved by the use of dedicated algorithms that adapt model parameters to a set of input variables

(namely: heart rate, cardiac output, arterial pressure, atrial pressure and, if available, ventricular volumes) through a recursive procedure. The heterogeneity of clinical data has been considered in developing the algorithm: it is conceived to adapt itself to the patient's status with different levels of confidence, depending on the available data and their accuracy.[8] The models are conceived to take into account the heterogeneity of clinical data: they can be set using different type of data both from catheterization and from echo.[19,21,22]

Finally, the educational functionalities rely on a pathology random generator, on a set of therapies (drugs, total blood volume control, mechanical circulatory assistance) and, additionally, on a remote control feature[8] to use the modelling platform within a learning management system.

The model equations are solved by Euler's method. It was adopted for its adaptability to real time equation solving, necessary for hybrid applications.[15] The solution of lumped parameters model equations is rather simple as it is based on the application of the basic circuital laws. The heart modules are composed of atrial and ventricular modules. Different selections are possible when starting the model: passive (simple compliance) or active (variable elastance model) atria, simple ventricles based on a single variable elastance model or more complex ventricles used for biventricular pacing simulation where two or three variable elastance models work in parallel, reproducing ventricular walls and septum.[9] Heart models include a set of heart valve models – from a simple diode to backflow models[7] to models including leaflet movements.[23]

Finally, the modelling platform can be connected to physical or computational mechanical heart assist devices: they include continuous or pulsatile flow devices and intra aortic balloon pump.[19,25]

The data storing procedure and content of the generated files will be described in the next paragraph.

Data Records

The data storing procedure is embedded in the modelling platform and generates Excel datasheet files that can be easily exported. The data storing procedure has two options: the first one is to create an excel data file containing the full set of variables generated by the model along with the ventricular and circulatory parameters. The user can select the number of cardiac cycles to be stored and has the option to select data averaged in the cardiac cycle or the full set of data points (by default sampled at 1 msec). The second storing option permits to build a personalised data file where only the variables of interest are stored. The data file is in Excel format as in the first storing option.

Stored data files are divided into different areas as it follows. The file described here was obtained performing a simulation from a physiological condition to a pathological one, finally assisted by a continuous flow pump. The used configuration corresponds to the basic, simpler version of the model. Some of the data in the file are necessary for the model check. What will be described here are only the data of interest to clinical use:

1. General information: version of the software, release date, place, date and time of the acquisition.
2. Heart rate [bpm] and systole-diastole ratio
3. Circulatory parameters. The parameters in *Italic* can be adjusted by the user.
- *Cas [$cm^3 \cdot mmHg^{-1}$]: systemic arterial compliance;*
- Ls [$g \cdot cm^{-4}$]: systemic arterial inertance;
- Rcs [$g \cdot cm^{-4} \cdot s^{-1}$]: systemic arterial characteristic resistance;
- *Rper [$g \cdot cm^{-4} \cdot s^{-1}$]: arterial systemic arterial resistance;*
- *Cvs [$cm^3 \cdot mmHg^{-1}$]: systemic venous compliance;*
- *Rvs [$g \cdot cm^{-4} \cdot s^{-1}$]: systemic venous resistance;*
- *Cra [$cm^3 \cdot mmHg^{-1}$]: right atrial compliance;*
- *Cap [$cm^3 \cdot mmHg^{-1}$]: pulmonary arterial compliance;*
- Lp [$g \cdot cm^{-4}$]: pulmonary arterial inertances;
- Rcp [$g \cdot cm^{-4} \cdot s^{-1}$]: pulmonary arterial characteristic resistance;
- *Rpolm [$g \cdot cm^{-4} \cdot s^{-1}$]: pulmonary arterial resistance;*
- *Cap [$cm^3 \cdot mmHg^{-1}$]: pulmonary arterial compliance;*
- Rvp [$g \cdot cm^{-4} \cdot s^{-1}$]: pulmonary venous resistance;
- *Cla [$cm^3 \cdot mmHg^{-1}$]: left atrial compliance*

4. Ventricular parameters. The parameters in *Italic* can be adjusted by the user.
- *LVinv [$g \cdot cm^{-4} \cdot s^{-1}$]: mitral valve resistance*
- *LVinvr [$g \cdot cm^{-4} \cdot s^{-1}$]: mitral valve reverse resistance*
- *LVoutv [$g \cdot cm^{-4} \cdot s^{-1}$]: aortic valve resistance*
- *LVoutvr [$g \cdot cm^{-4} \cdot s^{-1}$]: aortic valve reverse resistance*
- *RVinv [$g \cdot cm^{-4} \cdot s^{-1}$]: tricuspid valve resistance*

- *RVinvr [g·cm^{-4}·s^{-1}]: tricuspid valve reverse resistance*
- *RVoutv [g·cm^{-4}·s^{-1}]: pulmonary valve resistance*
- *RVoutvr [g·cm^{-4}·s^{-1}]: pulmonary valve reverse resistance*
- Left ventricular filling and ejection parameters (they relate ventricular pressure and volume and control the rate of filling and ejection. In general, they are not user accessible with the exception of LVemax and LVv0): LVfil-al; LVfil-bl; LVfilcl; LVfildl; LVej-c1;LVej-c2;LVej-c3; *LVemax [mmHg·cm^{-3}]; LVv0 [cm^3].*
- Right ventricular filling and ejection parameters (they relate ventricular pressure and volume and control the rate of filling and ejection. In general, they are not user accessible with the exception of RVemax and RVv0): RVfil-ar; RVfil-br; RVfil-cr; RVfil-drl; RVej-c1; RVej-c2;RVej-c3; *RVemax [mmHg·cm^{-3}]; RVv0 [cm^3].*

5. Coronary parameters
6. Ventricular volumes:

- Vedl [cm^3]: left ventricular end-diastolic volume
- Vesl [cm^3]: left ventricular end-systolic volume
- SVl [cm^3]: left ventricular stroke volume
- Vedr [cm^3]: right ventricular end-diastolic volume
- Vesr [cm^3]: right ventricular end-systolic volume
- SVr [cm^3]: right ventricular stroke volume

7. Flows

- Qil [l·min^{-1}]: left ventricular input flow
- Qol [l·min^{-1}]: left ventricular output flow
- Qir [l·min^{-1}]: right ventricular input flow
- Qor [l·min^{-1}]: right ventricular output flow
- Qas [l·min^{-1}]: systemic arterial flow
- Qap [l·min^{-1}]: pulmonary arterial flow

8. Ventricular energetics

- EWl [J]: left ventricular external work
- VO2l [J]: left ventricular oxygen consumption
- CMEl: left ventricular cardiac mechanical efficiency
- PEl [J]: left ventricular potential energy
- EWr [J]: right ventricular external work
- VO2r [J]: right ventricular oxygen consumption
- CMEr: right ventricular cardiac mechanical efficiency
- Per [J]: right ventricular potential energy

9. Cardiac indexes and arterial elastances

- BSA: body surface area [m^2]
- CI [l·min^{-1}·m^{-2}]: cardiac index
- EF [%]: ejection fraction
- Eal [mmHg·cm^{-3}]: systemic arterial elastance
- Ear [mmHg·cm^{-3}]: pulmonary arterial elastance
- Pesl [mmHg]: left ventricular end-systolic pressure
- Pesr [mmHg]: right ventricular end systolic pressure
- Vtot [cm^3]: total blood volume

10. Continuous flow pump general parameters
11. Hemodynamic average data (in the cardiac cycle)

- Pas [mmHg]: mean aortic pressure
- PasM [mmHg]: systolic aortic pressure
- Pasm [mmHg]: diastolic aortic pressure
- Pvs [mmHg]: systemic venous pressure
- Pra [mmHg]: right atrial pressure
- Pap [mmHg]: pulmonary arterial pressure
- Pvp [mmHg]: pulmonary venous pressure
- Pla [mmHg]: left atrial pressure

12. Pneumatic ventricle parameters
13. Instantaneous data

- Time [s]
- plv [mmHg]: left ventricular pressure
- pas [mmHg]: aortic pressure
- pvs [mmHg]: systemic venous pressure
- pra [mmHg]: right atrial pressure
- prv [mmHg]: right ventricular pressure
- pvp [mmHg]: pulmonary venous pressure
- pla [mmHg]: left atrial pressure
- qli [cm^3·s^{-1}]: left ventricular input flow
- qlo [cm^3·s^{-1}]: left ventricular output flow
- vlv [cm^3]: left ventricular volume
- qri [cm^3·s^{-1}]: right ventricular input flow
- qro [cm^3·s^{-1}]: right ventricular output flow
- vrv [cm^3]: right ventricular volume
- the columns after vlv contain data for upper body/lower body configurations (not used in this experiment), pneumatic ventricle and continuous flow pump (used in this experiment).

Validation

The modelling platform was applied so far to different clinical problems having in common the use of the model to analyse complex pathophysiological situations and evaluate the effects of different approaches to the problem. Each application has been preceded by a model verification starting from a baseline condition. The Table 1 below summarizes the applications.

Table 1. Model applications and their verification.

Areas of application	Usage	Structure	Remote	Reference
Bi-ventricular pacing	C/R	Computational	N	[13],[24]
VAD conduction	C/R	Hybrid/Computational	Y	[8],[19]
IABP conduction	R	Hybrid	N	[25]
Congenital heart disease	C/R	Computational	Y	[9]
Paediatric VAD	C/R	Computational/Hybrid	Y	[19],[21],[22]
Educational Application	E	Computational/Hybrid	Y	[8]

Usage Legend: C-Clinical support, R-Research, E-Education

Use and Potential Reuse

The model output in the form of an excel file has been exploited for the applications outlined in Table 1 for retrospective and prospective data analysis. The use of the model for clinical support in fact permits to reproduce patient's status and simulate, starting from this point, the effects of different clinical choices. From educational point of view, the schema is the following:

- The trainee sees the model graphical interface, similar to a clinical monitor, and can chose between the generation of preset and known pathologies or can use the pathology random generator. The preset pathologies include valve defects and the main cardiocirculatory pathologies.
- When the trainee identifies a pathological situation, he or she can decide to adopt a clinical strategy based on drugs, surgical procedure or on a mechanical assistance.
- On the basis of the chosen actions, the trainee can modify the amount of drugs or the conduction of the mechanical assistance to improve hemodynamic conditions.

The remote access to the simulator is based on a different procedure if the simulator is fully computational or hybrid. In the latter case, the support of an operator is necessary to manage the VAD. In the case of computational models, the access is through the remote control software using a TCP-IP protocol.

Conclusions

The usage of models outlined in this paper is not totally new but it is the first time that models are organised in a platform where the user can chose the optimal configuration for the specific application. Furthermore, the graphical user interface offers a user friendly environment. The next developments of the platform will include a respiratory module (including pulmonary mechanics and gas exchange and transport). The remote accessibility to the models will be improved and made available for a multiuser environment.

Data Files

The data described in this paper is presented in an openly accessible spreadsheet: "*01303_Cardio-circulatory_pathologies.xls.*"

The file is available also in the Open Document Spreadsheet format.

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References

1. Pepper JR. Update on mechanical circulatory support in heart failure. Heart 2012;98:663-69. doi: 10.1136/heartjnl-2011-300735.

2. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson L, Miller M, Young JB. Long-term mechanical circulatory support (destination therapy): on track to compete with heart transplantation? J Thorac Cardiovasc Surg. 2012;144:584-603. doi: 10.1016/j.jtcvs.2012.05.044.

3. Gingrich KJ, Roy RJ. Modeling the hemodynamic response to dopamine in acute heart failure. IEEE Trans Biomed Eng. 1991;38(3):267-272. doi: 10.1109/10.133208.

4. Heldt T, Mukkamala R, Moody GB, and Mark RG. CVSim. An Open-Source Cardiovascular Simulator for Teaching and Research. Open Pacing Electrophysiol Ther J. 2010;3:45–54. PMID: 21949555.

5. Goodwin A, van Meurs WL, Sá Couto CD, Beneken JE, Graves SA. A model for educational simulation of infant cardiovascular physiology. Anesth. Analg. 2004;99(6):1655-64. doi 10.1213/01.ANE.0000134797.52793.AF.

6. Tokaji M, Ninomiya S, Kurosaki T,Orihashi K, Sueda T. An Educational Training Simulator for Advanced Perfusion Techniques Using a High-Fidelity Virtual Patient Model. Artificial Organs 2012;36(12): 1026–35. doi: 10.1111/j.1525-1594.2012.01512.x.

7. Ferrari G, Kozarski M, Gu YJ, De Lazzari C, Di Molfetta A, Pałko KJ, Zieliński K, Górczyńska K, Darowski M, Rakhorst G. Application of a user friendly comprehensive circulatory model for hemodynamic and ventricular variables estimate. Int J Artif Organs 2008;31:1043-54. PMID: 19115196.

8. Fresiello L, Ferrari G, Di Molfetta A, Zieliński, K, Tzallas A, Jacobs S, Darowski M, Kozarski M, Meyns B, Katertsidis NS, Karvounis EC, Tsipouras MG, Trivella MG. A cardiovascular simulator tailored for training and clinical uses. Journal of Biomedical Informatics, 2015; 57:100-112. doi: 10.1016/j.jbi.2015.07.004.

9. Di Molfetta A, Jacobs S, Fresiello L, Verbelen T, Trivella MG, Meyns B, Ferrari G. Simulation of apical and atrio-aortic VAD in patients with transposition or congenitally corrected transposition of the great arteries. Int. J. Artif. Organs 2014;37(1):58-70. doi: 10.5301/ijao.5000264.

10. Di Molfetta A, Pilati M, Fresiello L, Amodeo A, Cristofaletti A, Pongiglione G, Gagliardi MG, Ferrari G. Tailoring the hybrid palliation for hypoplastic left heart syndrome: A simulation study using a lumped parameter model. Medical Engineering & Physics, 2015;37(9): 898-904. doi: 10.1016/j.medengphy.2015. 04.012

11. Di Molfetta A, Amodeo A, Fresiello L, Trivella MG, Iacobelli R, Pilati M and Ferrari G. Simulation of Ventricular, Cavo-Pulmonary, and Biventricular Ventricular Assist Devices in Failing Fontan. Artificial Organs 2015;39(7):550–558. doi: 10.1111/aor.12434.

12. Ferrari G, Khir AW, Fresiello L, Di Molfetta A and Kozarski M. Hybrid model analysis of IABP performance as a function of ventricular and circulatory parameters. Artificial Organs 2011;35(9):902-11. doi: 10.1111/ j.1525-1594.2011.01244.x.

13. Di Molfetta A, Cesario M, Tota C, Santini L, Forleo GB, Sgueglia M, Ferrari G, Romeo F. Use of a comprehensive numerical model to improve biventricular pacemaker temporization in patients affected by heart failure undergoing to CRT-D therapy. Medical & Biological Engineering & Computing 2010;48(8):755-64. doi: 10.1007/s11517-010-0623-0.

14. Mahmood MN, Fresiello L, Di Molfetta A, Ferrari G. A modelling tool to study the combined effects of drug administration and LVAD assistance in pathophysiological circulatory conditions. Int J Artif Organs 2014; 37(11): 824 – 833. doi: 10.5301/ ijao.5000366.

15. Ferrari G, Kozarski M, De Lazzari C, Clemente F, Merolli M, Tosti G, Guaragno M, Mimmo R, Ambrosi D, Głapinski J. A hybrid (numerical-physical) model of the left ventricle. The International Journal of Artificial Organs 2001;24(7), 456-62. PMID: 11510917.

16. Kozarski M, Ferrari G, Zieliński K, Górczyńska K, Pałko KJ, Tokarz A, Darowski M. A New Hybrid Electro-Numerical Model of the Left Ventricle. Computers in Biology and Medicine 2008;38(9),979-89. Doi: 10.1016/j.compbiomed.2008.07.001.

17. Kozarski M, Ferrari G, Zieliński K, Górczyńska K, Pałko KJ, Fresiello L, Di Molfetta A, Darowski M. A hybrid (Hydro-Numerical) Cardiovascular Model Application to Investigate Continuous-Flow Pump Assistance Effect. Biocybernetics and Biomedical Engineering 2012;32(4):77-91. Doi: 10.1016/S0208-5216(12)70051-7.

18. Darowski M, Kozarski M, Ferrari G, Zielinski K, Górczyñska K, Szczepanowski A, Palko KJ, Fresiello L, Di Molfetta A. A new hybrid (hydro-numerical) model of the circulatory system. Bulletin of the Polish Academy of Sciences - Technical Sciences 2013; 61(4): 993-1003. doi: 10.2478/bpasts-2013-0107.

19. Fresiello L, Zielinski K, Jacobs S, Di Molfetta A, Palko KJ, Bernini F, Martin M, Ferrari G, Trivella MG, Gorczynska K, Darowski M, Meyns B and Kozarski M. Reproduction of continuous flow LVAD experimental data by means of a hybrid cardiovascular model with baroreflex control. Artificial Organs 2014; 38(6):456-68. doi: 10.1111/aor.12178.

20. Di Molfetta A, Ferrari G, Filippelli S, Fresiello L, Iacobelli R, Gagliardi MG and Amodeo A. The use of VAD in univentricular physiology: the role of lumped parameter models. Artif Organs, 2015. doi: 10.1111/aor.12583.

21. Di Molfetta A, Amodeo A, Fresiello L, Filippelli S, Pilati M, Iacobelli R, Adorisio R, Colella D, Ferrari G. The use of a numerical model to simulate the cavo-pulmonary assistance in Fontan circulation: a preliminary verification. Journal of Artificial Organs, 2015. doi: 10.1007/s10047-015-0874-5.

22. Di Molfetta A, Amodeo A, Gagliardi MG, Trivella MG, Fresiello L, Filippelli S, Toscano A and Ferrari G. Haemodynamic effects of VAD implantation on Norwood, Glenn and Fontan Circulation: a simulation study. Artificial Organs, 2015. doi: 10.1111/aor.12591.

23. Korakianitis T, Shi Y. A concentrated parameter model for the human cardiovascular system including heart valve dynamics and atrioventricular interaction. Med Eng Phys 2006;28:613–628. doi: 10.1016/ j.medengphy.2005.10.004.

24. Di Molfetta A, Santini L, Forleo G, Minni V, Mafhouz K, Della Rocca D, Fresiello L, Romeo F, Ferrari G. Towards a personalized and dynamic CRT-D: a computational cardiovascular model dedicated to therapy optimization. Methods of Information in Medicine 2012;51(6):495-506. doi: 10.3414/ME12-01-0011.

25. Fresiello L, Khir AW, Di Molfetta A, Kozarski M and Ferrari G. Effects Of Iabp Timing On Baroreflex Activities In A Closed Loop Cardiovascular Hybrid Model. Artificial Organs 2013;37:237-47. doi: 10.1111/ j.1525-1594.2012.01540.x.