Patient-specific models in human physiology

Yuri Vassilevski

INM RAS

dedicated to the 90th anniversary of G.I.Marchuk

June 9, 2015

Working group on mathematical models and numerical methods in biomathematics

Supported by G.I.Marchuk

- Informal society of modelers and mathematicians since 2010
- Activities
  - Series of workshops
  - Special issues in international journals
  - Website *dodo.inm.ras.ru/biomath*

Working group on mathematical models and numerical methods in biomathematics

Series of workshops at INM RAS

1. 15-16 June 2010: 16 talks
2. 11-12 January 2011: 18 talks
3. 27-28 October 2011: 21 talks
4. 11-12 October 2012: 20 talks
5. 29-30 October 2013: 24 talks
6. 29-31 October 2014: 41 talks 4th workshop MMM in biology and medicine

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The next conference will be in the end of October 2015.

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Special issues of journals

Peer-reviewed papers in

1. Math.Modelling of Natural Phenomena 6, No.7, 2011
2. Rus. J. Numer.Analysis and Math.Modelling 26, No.6, 2011
3. Rus. J. Numer.Analysis and Math.Modelling 27, No.5, 2012
4. Rus. J. Numer.Analysis and Math.Modelling 28, No.5, 2013
5. Rus. J. Numer.Analysis and Math.Modelling 29, No.5, 2014

dodo.inm.ras.ru/biomath

Personalized models of physiological processes

Future of medicine is treatment of an individual on the basis of tracking its immunologic, endocrinologic, vascular features

G.I.Marchuk

Personalized models of physiological processes

Basic issues:

- computational domain (human body, organs, tissues ...)

Personalized models of physiological processes

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- parameters, coefficients

Personalized models of physiological processes

Basic issues:

- computational domain (human body, organs, tissues ...)
- equations
- parameters, coefficients
- applications

Personalized models of physiological processes

Our team (co-authors):

- Sergey Simakov (MIPT, INM RAS)
- Alexander Danilov (INM RAS, MIPT)
- Maxim Olshanskii (University of Houston, INM RAS)
- Igor Konshin (CC RAS, INM RAS)
- German Kopytov (Baltic Federal University, INS RAS)
- Victoria Salamatova (MIPT, INM RAS)
- Tatiana Dobroserdova (INM RAS, MIPT)
- Yuri Ivanov (INM RAS, MIPT)
- Timur Gamilov (MIPT)
- Alexandra Yurova (MSU, MIPT)
- Vasily Kramarenko (MIPT)
- Nina Gorodnova (INM RAS)
- Roman Pryamonosov (MSU)

Personalized models of physiological processes

Our team is distributed:

- Moscow Institute of Physics and Technology
  - Chair of numerical mathematics
  - Chair of computational technologies and modelling
  - Laboratory of human phsysiology
- INM RAS
  - Working group for modelling of blood flows and vascular pathologies

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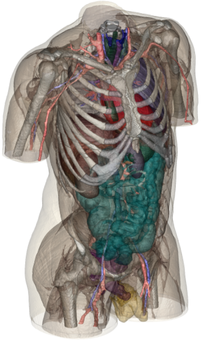
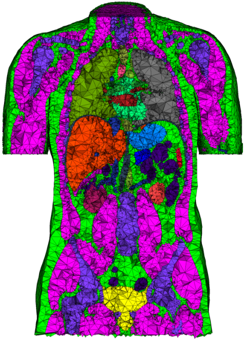
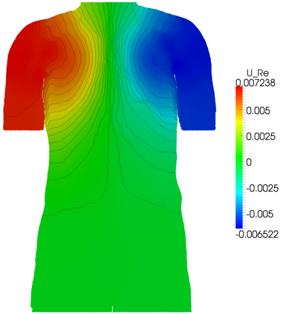
- Russian Science Foundation 2014-2016
- Federal Target Program "Academic and pedagogical staff of innovative Russia" 2010-2012
- Russian Foundation for Basic Research
- Russian Federation President Grants (2013-2016)

Technology overview

Segmentation | Meshing | FEM







ITK-SNAP | CGAL Mesh | Ani3D | ParaView

A. A. Danilov, D. V. Nikolaev, S. G. Rudnev, V. Yu. Salamatova and Yu. V. Vassilevski, Modelling of bioimpedance measurements: unstructured mesh application to real human anatomy. *Russ. J. Numer. Anal. Math. Modelling*, 2012 **27** (5), 431–440

Visible Human Project

Visible Human Project
U.S. National Library of Medicine
www.nlm.nih.gov/research/visible

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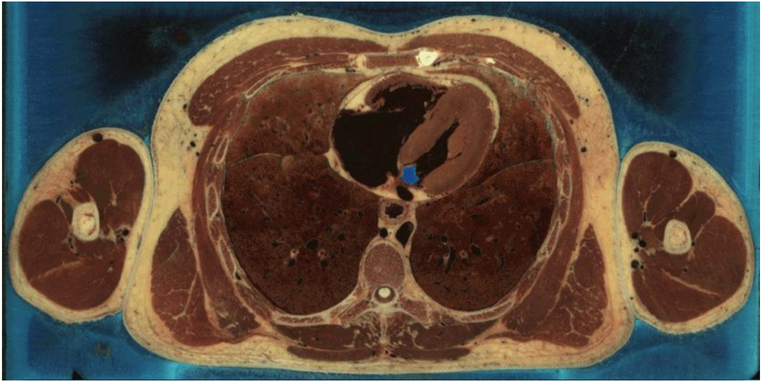
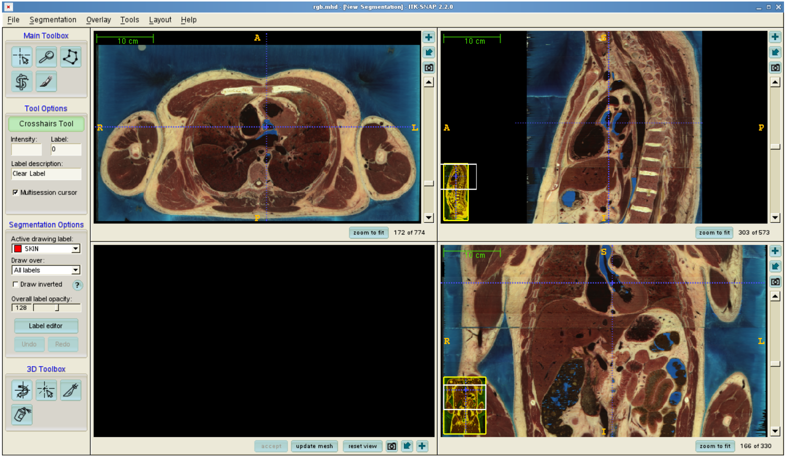


ITK-SNAP software

ITK-SNAP free software for Visualization and Segmentation

www.itksnap.org

manual and semi-automatic segmentation



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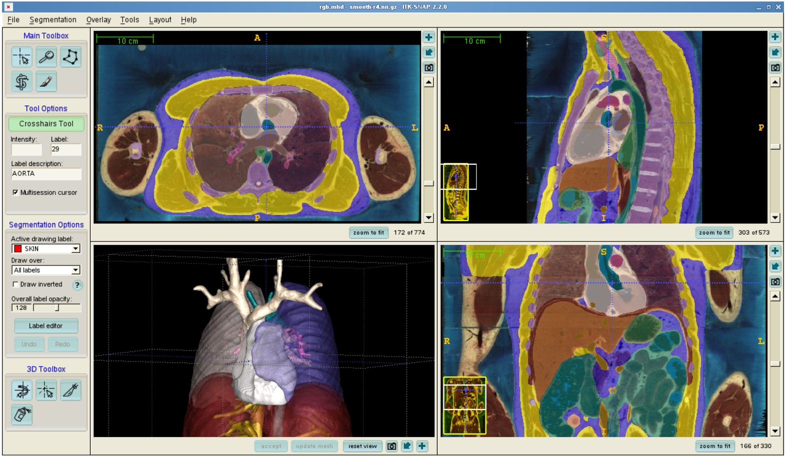
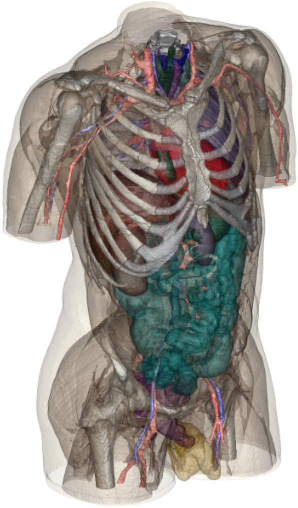
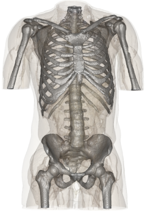
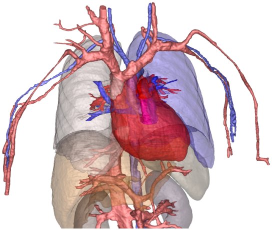


High resolution segmented model of VHP torso



567 $\times$ 305 $\times$ 843 voxels
1 $\times$ 1 $\times$ 1 mm
26 organs and tissues

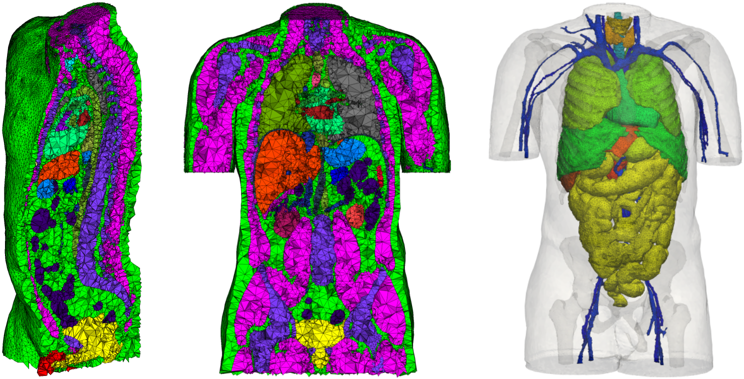




Total 146m voxels, 68m material voxels

Unstructured tetrahedral meshes

CGAL Mesh (`www.cgal.org`) – Delaunay mesh generation
Ani3D (`sf.net/p/ani3d`) – mesh cosmetics

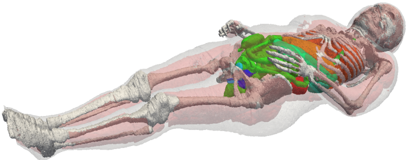


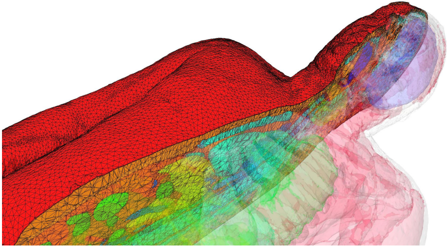
413 508 vertices, 2 315 329 tetraedra, 84 430 boundary faces

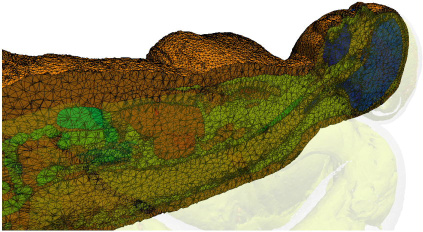
Full body male and female models

VHP-Man

VHP-Woman

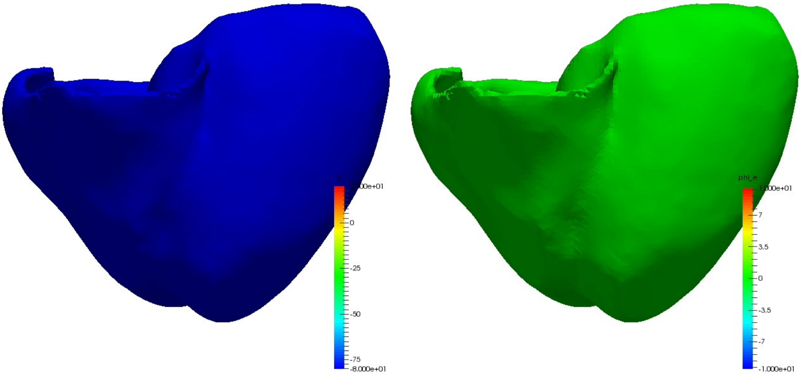






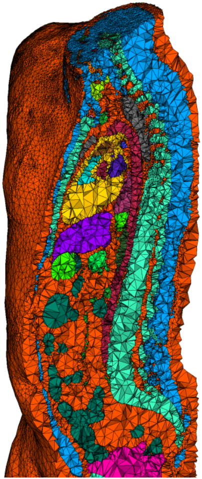
3m tetrahedra   effective resolution: $1 \times 1 \times 1$ mm   30 tissues

ECG model



Cardiac simulation using Chaste `www.cs.ox.ac.uk/chaste`

ECG model

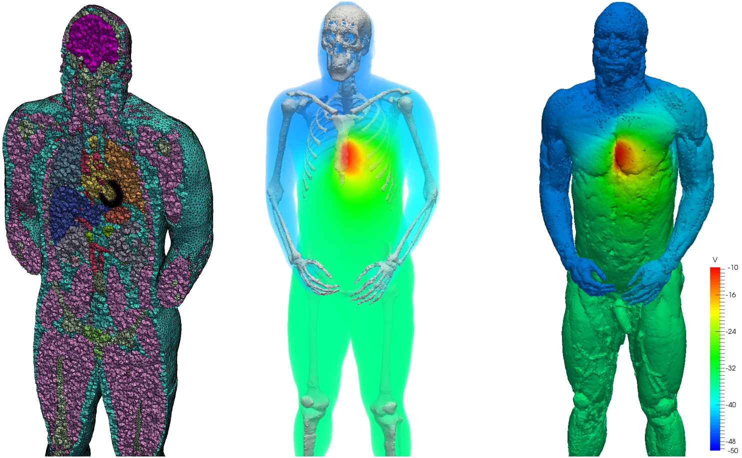


$$\begin{aligned} \mathrm{div}(\mathbf{C}\nabla U) = 0 \quad & \text{in} \quad \Omega \\ U = U_h \quad & \text{on} \quad \Gamma_h \\ \mathbf{J}_n = 0 \quad & \text{on} \quad \partial\Omega \setminus \Gamma_h \end{aligned}$$

U potential field
$\mathbf{C}$ conductivity tensor
$\mathbf{E} = \nabla U$ intensity field
$\mathbf{J} = \mathbf{C}\ \mathbf{E}$ current density field
Γ_h heart surface

ECG model

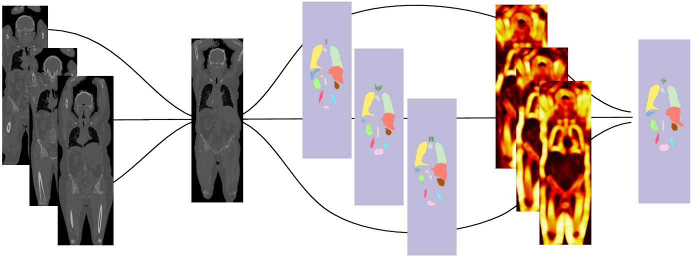
A.Danilov



Electrical potential field, 50ms after excitation

Personalized segmentation methods

1. Atlas based segmentation
2. Clustering and classification
3. Active contours and heuristics



Medical Computer Vision: Algorithms for Big Data
Lecture Notes in Computer Science, 2014, Vol. 8848

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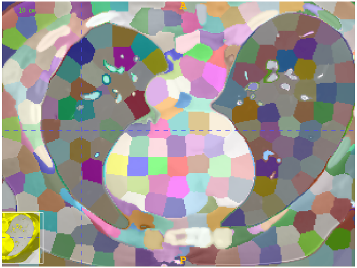

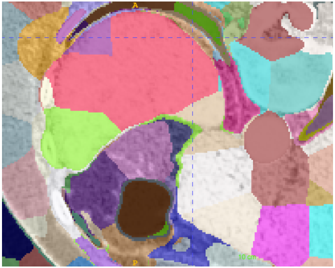

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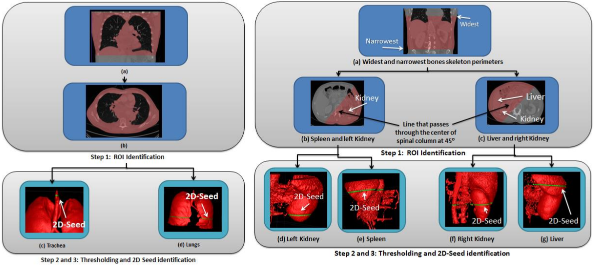

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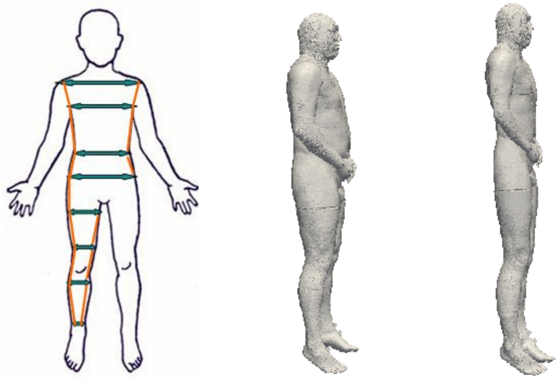
Patient specific models

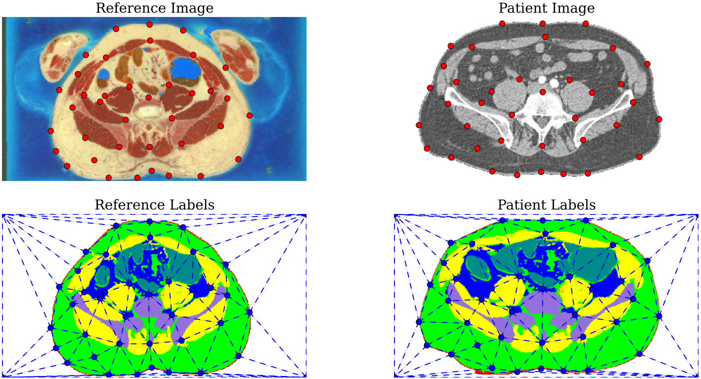
First step anthropometric adaptation



Simple fitting of the model

Control points adaptation

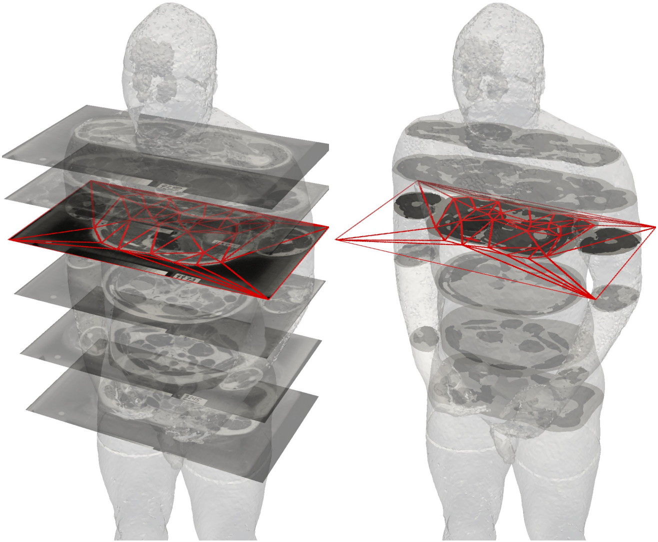
A.Danilov, A.Yurova



Piecewise affine mapping in control plane

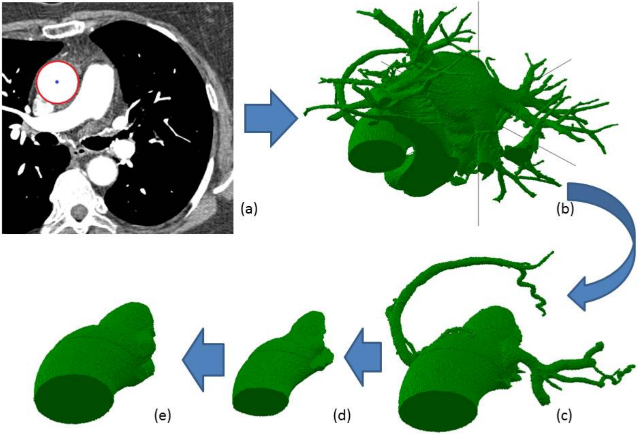
Control points adaptation

A.Danilov, A.Yurova



Coronary vessels extraction

R.Pryamonosov

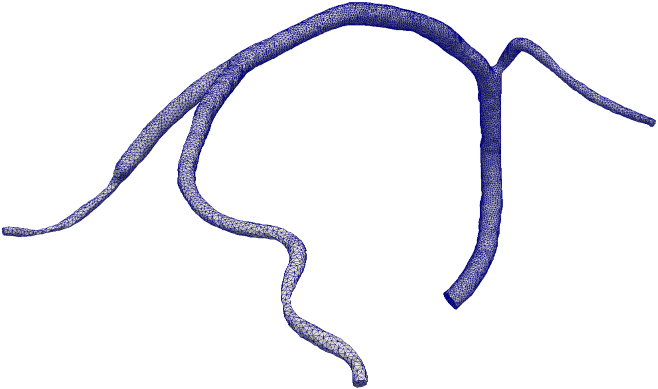


Aorta segmentation pipeline: (a) red circle corresponds to aorta cut, (b) connected initial mask, (c) output of isoperimetric distance trees contains a noisy aorta mask and parts of coronary vessels, (d) shrinking mask, (e) expanding mask provides the aorta segmentation.

Frangi vesselness filter detects ostia points and coronary vessels

Coronary vessels 3D mesh

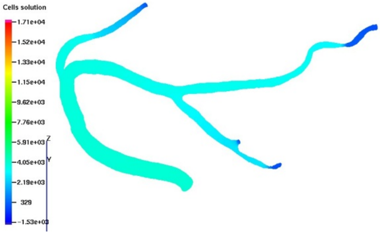
A.Danilov, T.Dobroserdova



63453 tetrahedra, 17153 vertices

Coronary vessels 3D mesh

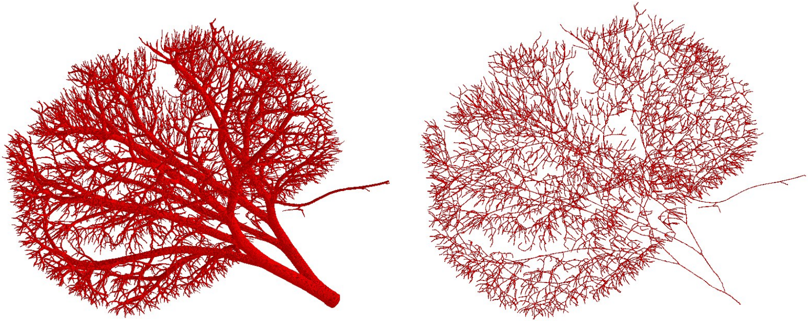
A.Danilov, T.Dobroserdova



pressure field at different time steps

Vessels sceletonization

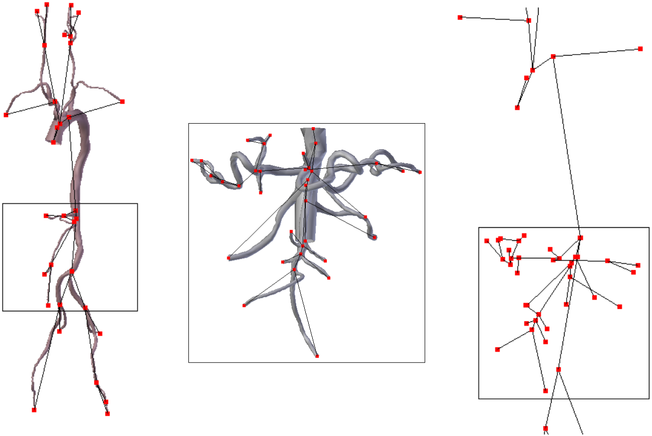
R.Pryamonosov



Fast and robust centerline extraction

Graph network extraction

Yu.Ivanov



Local graph adaptation

Hemodynamic equations

A.Kholodov, S.Simakov

Mass and momentum balance

$$\partial S_k/\partial t + \partial(S_k u_k)\,/\partial x = 0,$$
$$\partial u_k/\partial t + \partial\left(u_k^2/2 + p_k/\rho\right)/\partial x = f_{fr}(S_k, u_k)\,,$$

k is index of the tube, t is the time, x is the distance along the tube, ρ is the blood density (constant), $S_k(t, x)$ is the cross-section area, $u_k(t, x)$ is the linear velocity averaged over the cross-section, $p_k(S_k)$ is the blood pressure, f_{fr} is the friction force

Hemodynamic equations

A.Kholodov, S.Simakov

At the vessels junctions the Poiseuille's pressure drop and mass conservation

$$p_k\left(S_k\left(t,\tilde{x}_k\right)\right) - p^l_{node}\left(t\right) = \varepsilon_k R^l_k S_k\left(t,\tilde{x}_k\right) u_k\left(t,\tilde{x}_k\right), k = k_1, k_2, \ldots, k_M,$$

$$\sum_{k=k_1,k_2,\ldots,k_M} \varepsilon_k S_k\left(t,\tilde{x}_k\right) u_k\left(t,\tilde{x}_k\right) = 0,$$

$\varepsilon = 1, \tilde{x}_k = L_k$ for incoming tubes, $\varepsilon = -1$, and $\tilde{x}_k = 0$ for outgoing tubes, R^l_k is the hydraulic resistance

finite differences approximation of compatibility conditions along outgoing characteristics

Hemodynamic equations

A.Kholodov, S.Simakov

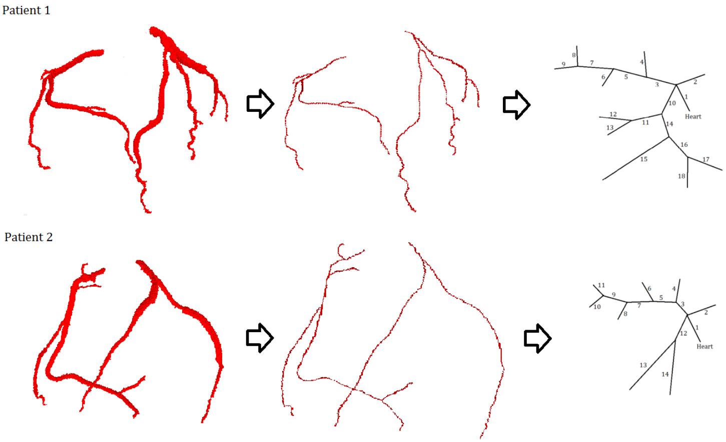
Elasticity of the tube wall:

$$p_k(S_k) - p_{*k} = \rho c_k^2 f(S_k)$$

Virtual fractional flow reserve

S.Simakov et al.

$$FFR = \frac{\overline{P}_{dist}}{\overline{P}_{aortic}}$$



Virtual fractional flow reserve

S.Simakov et al.

Vessel	Measured FFR	Virtual FFR	Difference
LAD-1	0.51	0.58	+14%
LCA-1	0.72	0.84	+17%
LCX-1	0.59	0.61	+3%
LAD-2	0.74	0.78	+5%
RCA-2	0.93	0.87	-5%

Thank you for your attention!