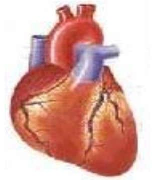
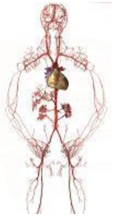

Numerical modeling of blood flow: applications to predictive endovascular surgery

Simakov Sergey[1,2]

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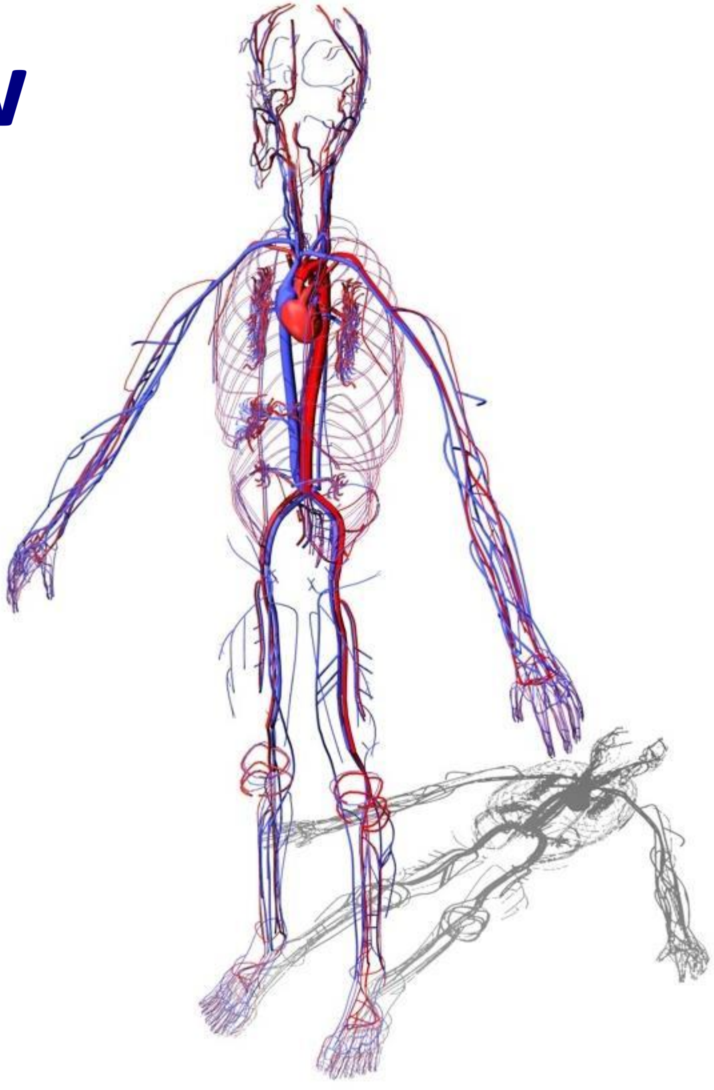
Grant No 14-31-00024 (New Laboratories)

(1) Moscow Institute of Physics and Technology
(2) Institute of Numerical Mathematics
Workgroup on modelling blood flow and vascular diseases

8th Conference on Mathematical Modelling and Computational Methods in Biomathematics
Moscow, INM RAS, 31.10.2016

1D Systemic Blood Flow Model



Global blood flow

1) Mass balance

$$\frac{\partial S}{\partial t}+\frac{\partial\left(uS\right)}{\partial x}=f_S$$

2) Momentum balance

2a) $$\frac{\partial u}{\partial t}+\frac{\partial}{\partial x}\left(\frac{u^2}{2}+\frac{P\left(S\right)}{\rho}\right)=f_u$$

2b) $$\frac{\partial Q}{\partial t}+\frac{\partial}{\partial x}\left(\frac{\alpha Q^2}{S}\right)+\frac{S}{\rho}\frac{\partial P}{\partial x}+K_R\frac{Q}{S}=f_Q$$

3) Junctions

3.1 $$\sum_{k=k_1,\ldots,k_M}\varepsilon_k^m u_k S_k=0,\varepsilon_k^m=\pm 1$$

3.2a $$p_k\left(S_k,x_k\right)-p_m^{node}=\alpha_k R_k^m u_k S_k,x_k=0,L_k$$

3.2b $$\frac{u_k^2\left(S_k,x_k\right)}{2}+\frac{p_k\left(S_k,x_k\right)}{\rho}=const$$

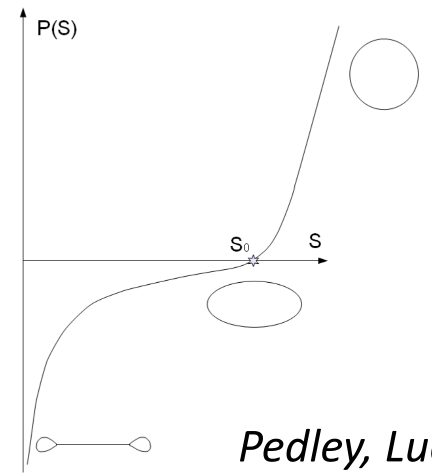
3.2c $$p_k\left(S_k,x_k\right)=p_m^{node}$$

Vessel wall elasticity

Analytic approximation

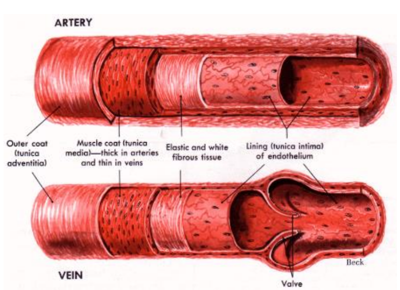
$$P(S) = P^{ext}(t,x) + \rho c^2 f(S)$$

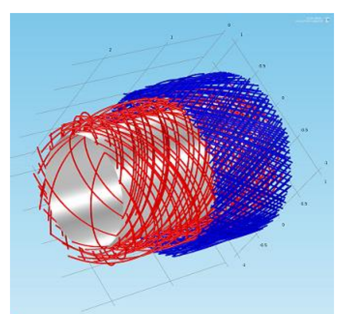
$$f(S) = \begin{cases} \exp(S/S_0 - 1) - 1, S > S_0 \\ \ln(S/S_0), S \le S_0 \end{cases}$$



Pedley, Luo, 1998

Modelling





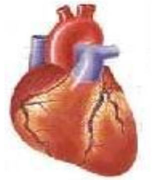
$$T = \sigma\vec{\xi} \quad \left(\vec{\xi} = \frac{\partial \vec{X}}{\partial s}\right)$$

$$\vec{f} = \frac{\partial}{\partial s}(T\vec{\tau}), \quad \vec{\tau} = \vec{\xi}/\left|\vec{\xi}\right|$$

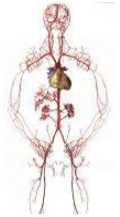
$$p = \left(\vec{f}, \vec{n}\right)h$$

$$\sigma\left(\vec{\xi}\right) = \begin{cases} T_*\left(\left|\vec{\xi}\right| - R_*\right), \left|\vec{\xi}\right| > R_*, \\ 0, \left|\vec{\xi}\right| \le R_* \end{cases}$$

Yu. Vassilevski, S Simakov, V. Salamatova, T. Dobroserdova, Blood Flow Simulation in Atherosclerotic Vascular Network Using Fiber-Spring Representation of Diseased Wall, Math. Mod. In Nat. Phenom., 6(5):333-349, 2011



Physiological conditions: autoregulation



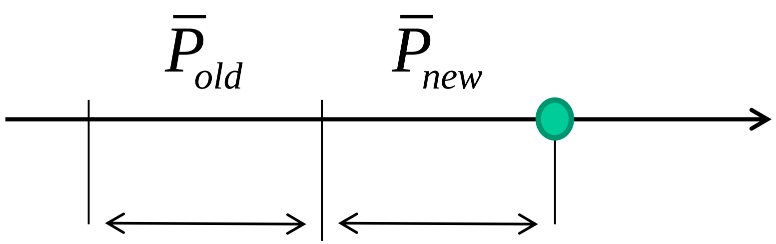
Wall elasticity adaptation to average pressure

Mechanism: endothelial layer permeability

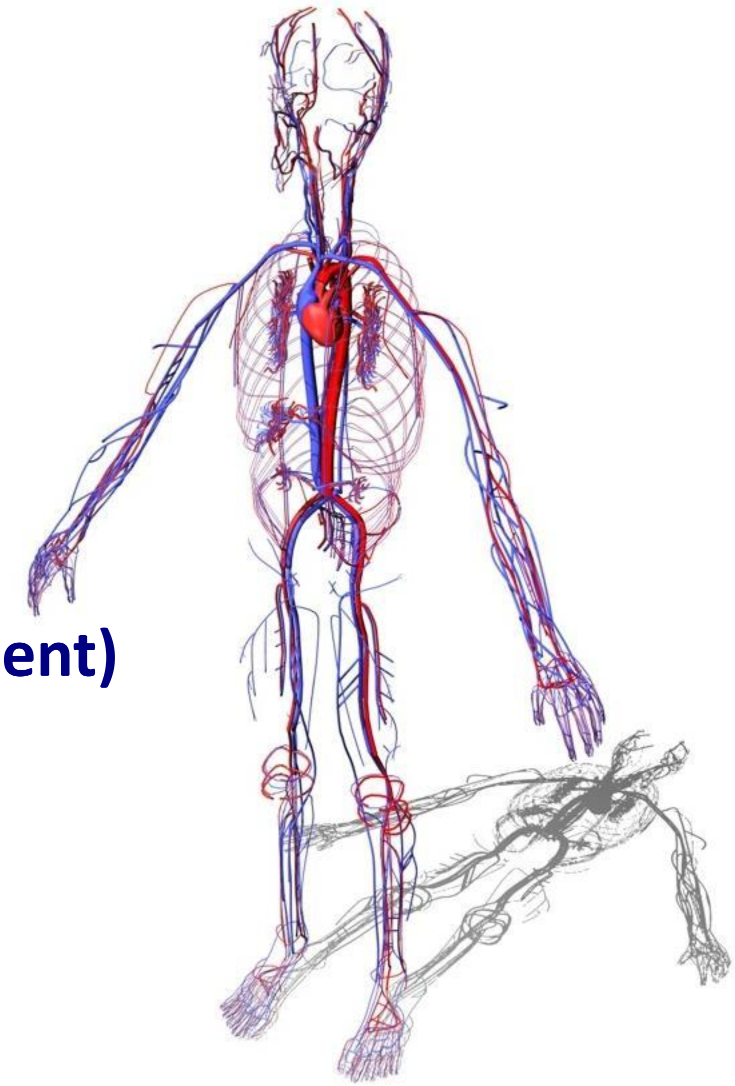
shear stress ↗ endothelial layer permeability ↘ NO production

$$P = \rho c^2 \left(\exp\left(\frac{S}{S_0} - 1 \right) - 1 \right)$$

$$\frac{c_{new}}{c_{old}} = \left(\frac{\bar{P}_{new}}{\bar{P}_{old}} \right)^{1/2}$$



Biomedical Applications:



- ✓ **Angiosurgery**
- ✓ **Fractional Flow Reserve**
- ✓ **Cerebral Flow (carotid stenosis treatment)**

General method for simulations

MRI/CT → 3D → 1D vascular structure

Ultrasound → Functional parameters fitting before surgery (elasticity, resistance, boundary conditions)

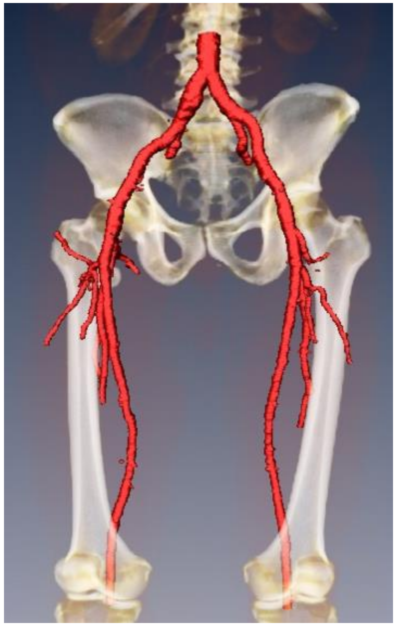
Heart rate
Arterial pressure
Age, Lifestyle … → Functional parameters fitting before surgery (elasticity, resistance, boundary conditions)

Virtual "surgery" → Predictive simulations of after surgery conditions

Angiosurgery (stenting)

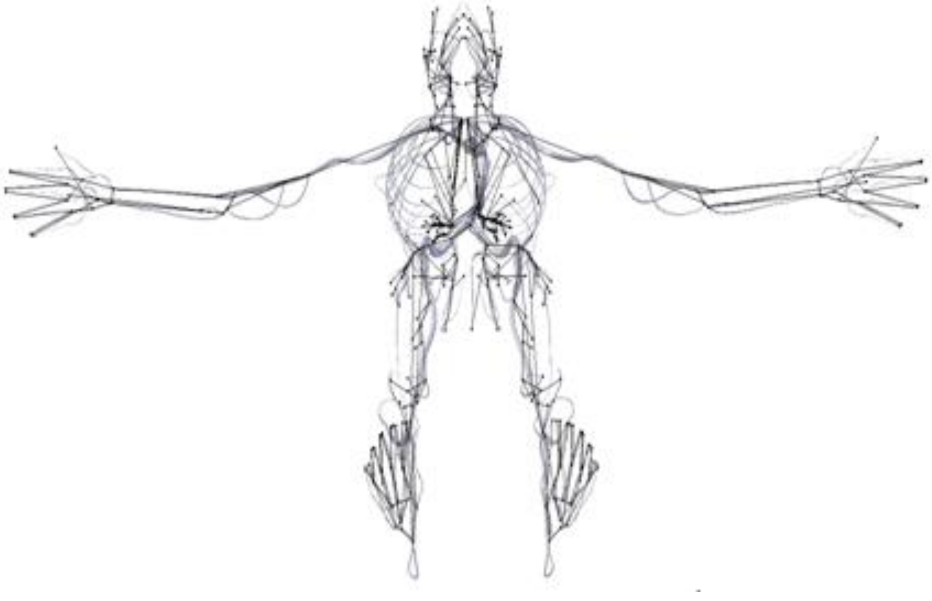
Vascular surgery: stenosis treatment

MRI/CT

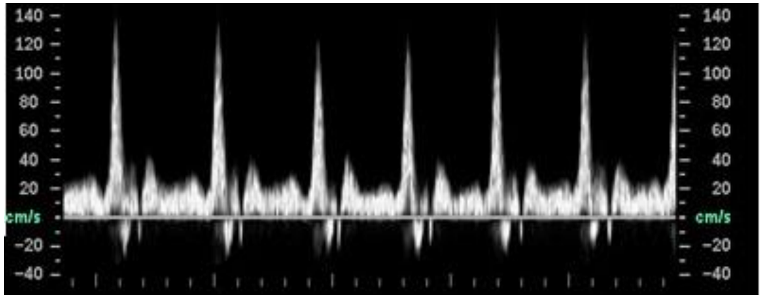


Computational model:

- 1D vascular structure
- Functional parameters fitting (elasticity, resistance)
- Simulations



Ultrasound dopplerography



Stenosis treatment: boundary conditions and identification

Boundary conditions

Input (arteries): $Q_{in} = \alpha Q_{heart}(t),$

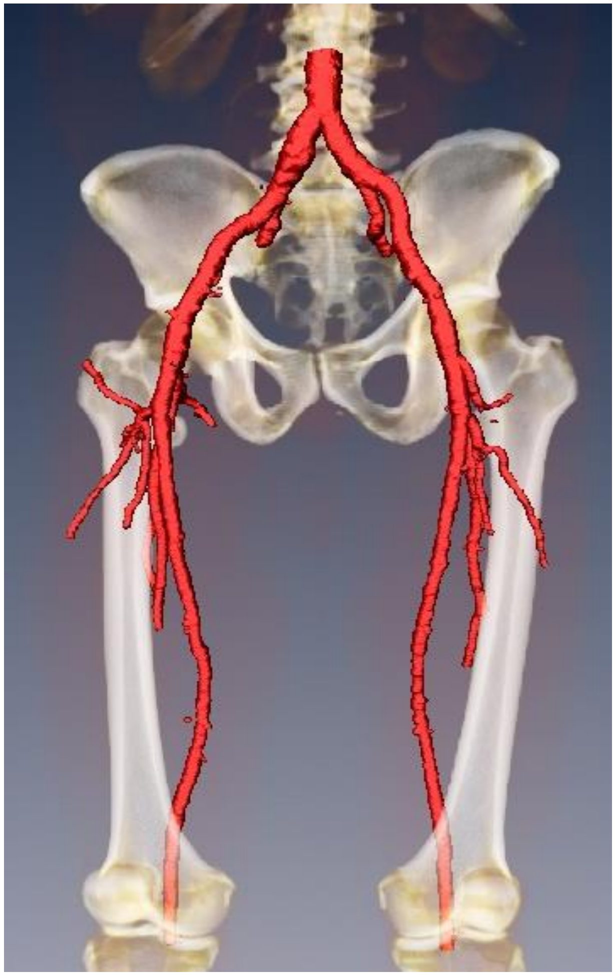
$\alpha = 0.21;$

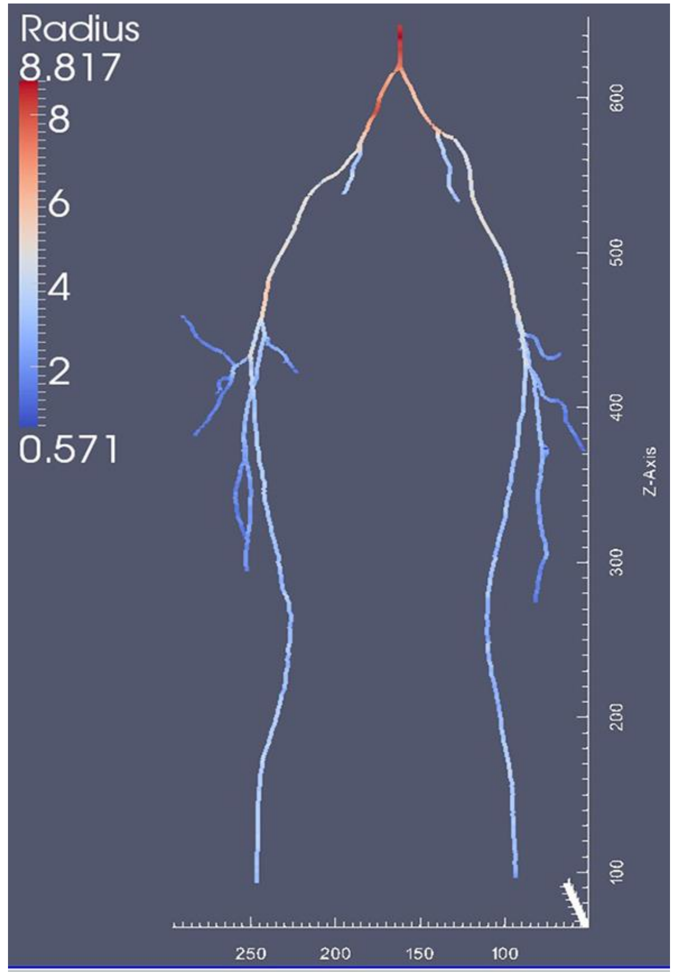
Output (veins): $Q_{out} = \overline{\alpha Q_{heart}(t)},$

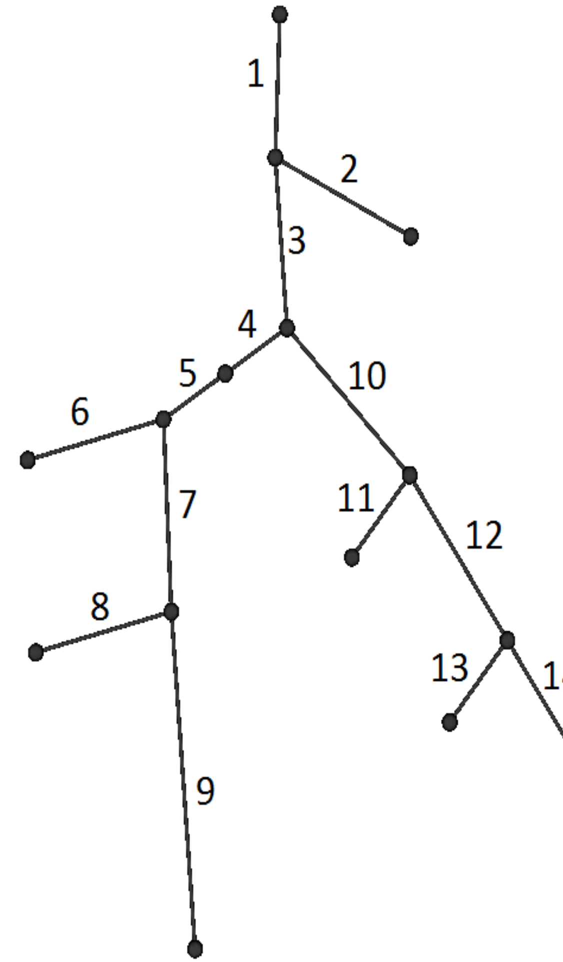
Parameters identification

- Ultrasound measurements (before surgery!)
- Angles between vessels at bifurcations
- Large vessels – rigid walls, small vessels – more elastic
- Occlusion – decreased lumen, high resistance

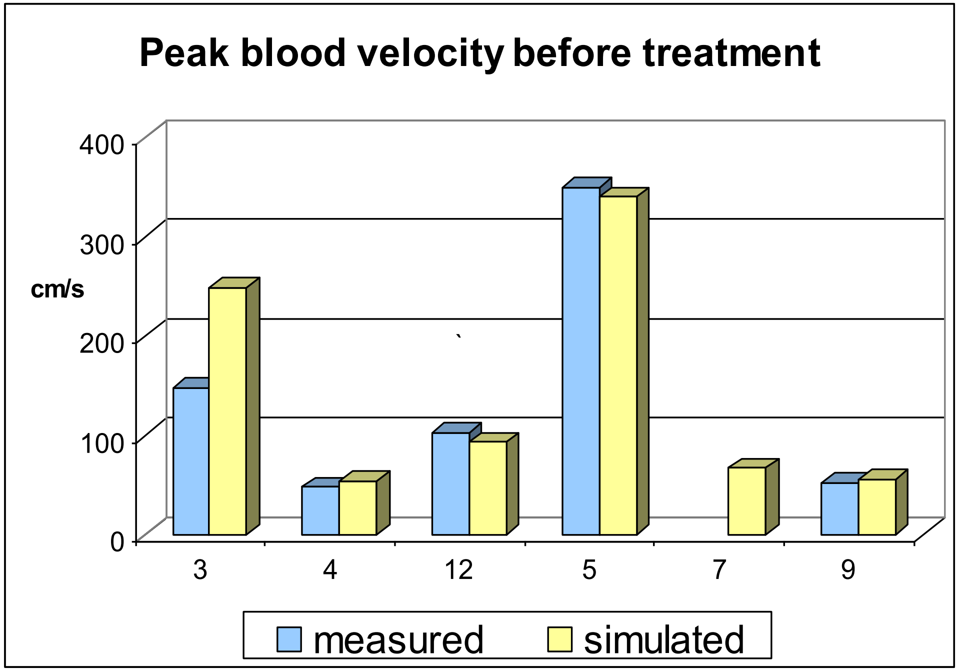
Stenosis treatment:
1D vascular domain reconstruction

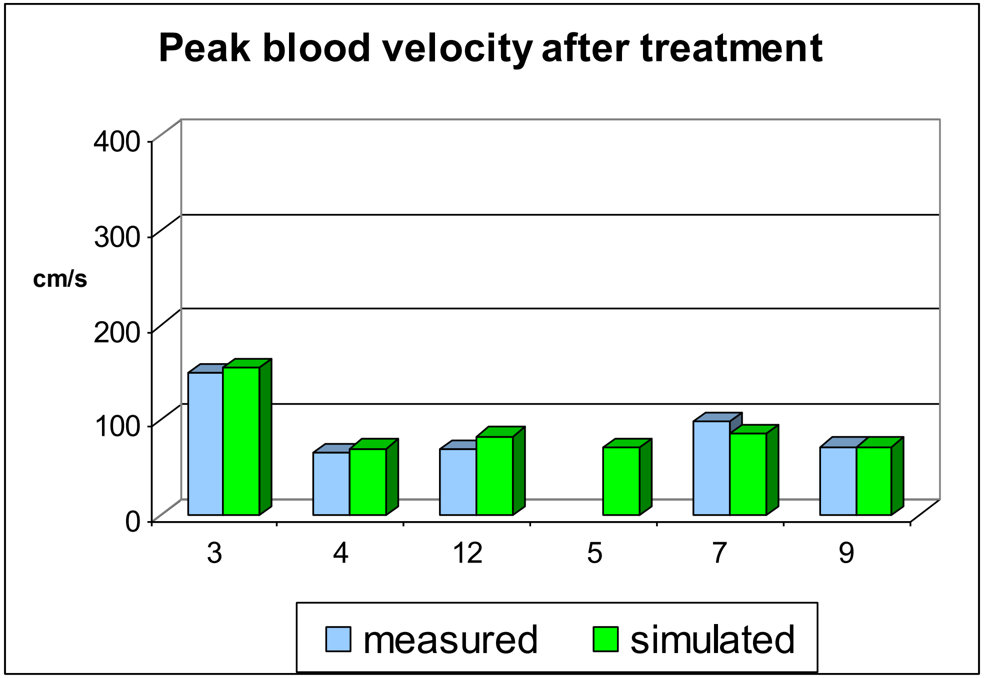






Stenosis treatment

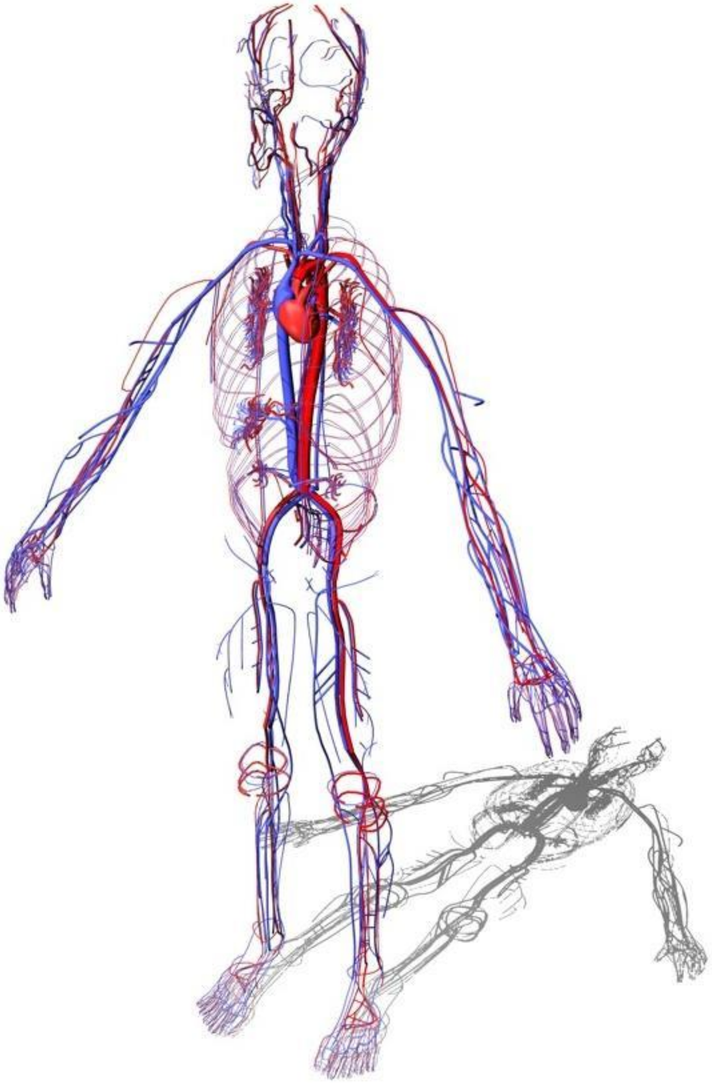




Patient-specific MRI and Doppler ultrasound data thanks to
I.M. Sechenov First Moscow State Medical University (Ph.Kopylov, et.al.)

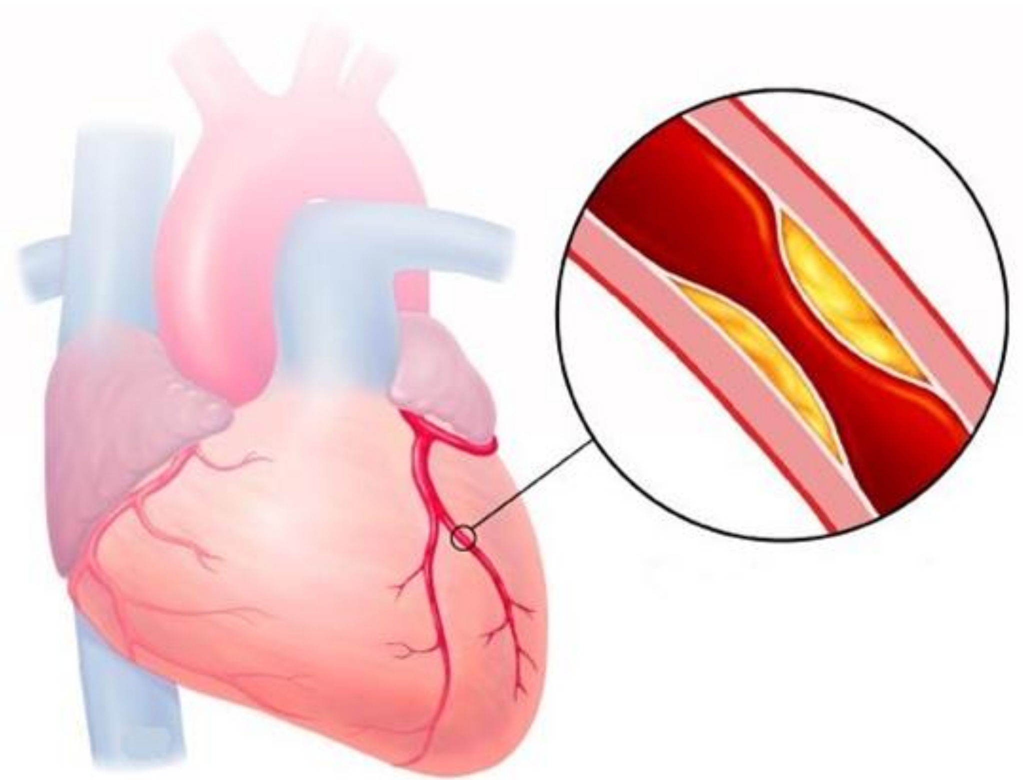
S.Simakov, T.Gamilov, Yu.Vassilevskii, Yu.Ivanov, P.Kopylov, Patient specific haemodynamics modeling after occlusion treatment in leg, Mat. Mod. Nat. Phen, 2014

Virtual Fractional Flow Reserve Assesment



Stenting of coronary arteries

Stenosis

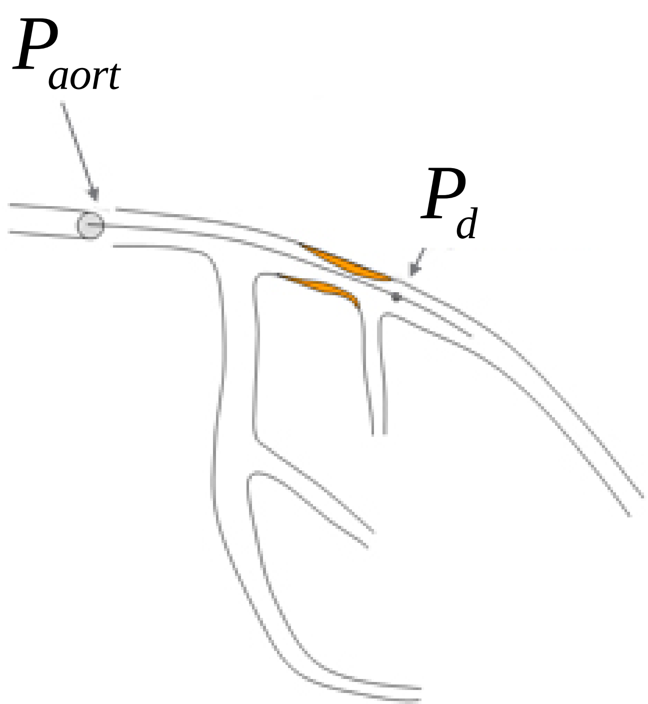


Treatment
- drugs
- surgery

Haemodynamical importance during single/multivessel diseases ???

Fractional flow reserve «Golden standard»

Vasodialtion → Maximum possible lumen



$$FFR = \frac{\text{pressure distal to the lesion } (P_d)}{\text{aortic pressure } (P_{aort})}$$

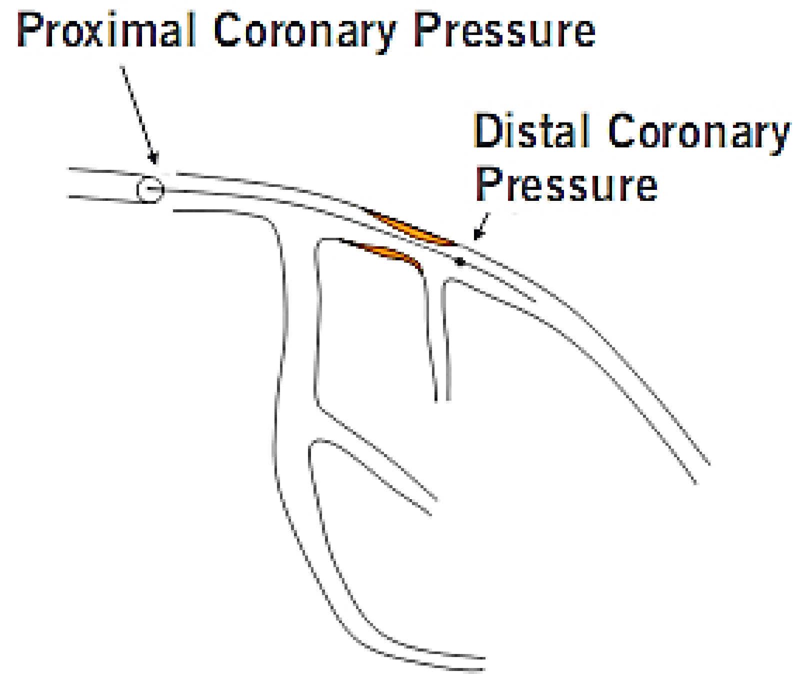
$FFR = 1$ → Normal value

FFR<0.75 → Revascularisation (stenting)

Fractional flow reserve (FFR)

$$FFR = \frac{\text{Distal Coronary Pressure}}{\text{Proximal Coronary Pressure}}$$

(During Maximum Hyperemia)



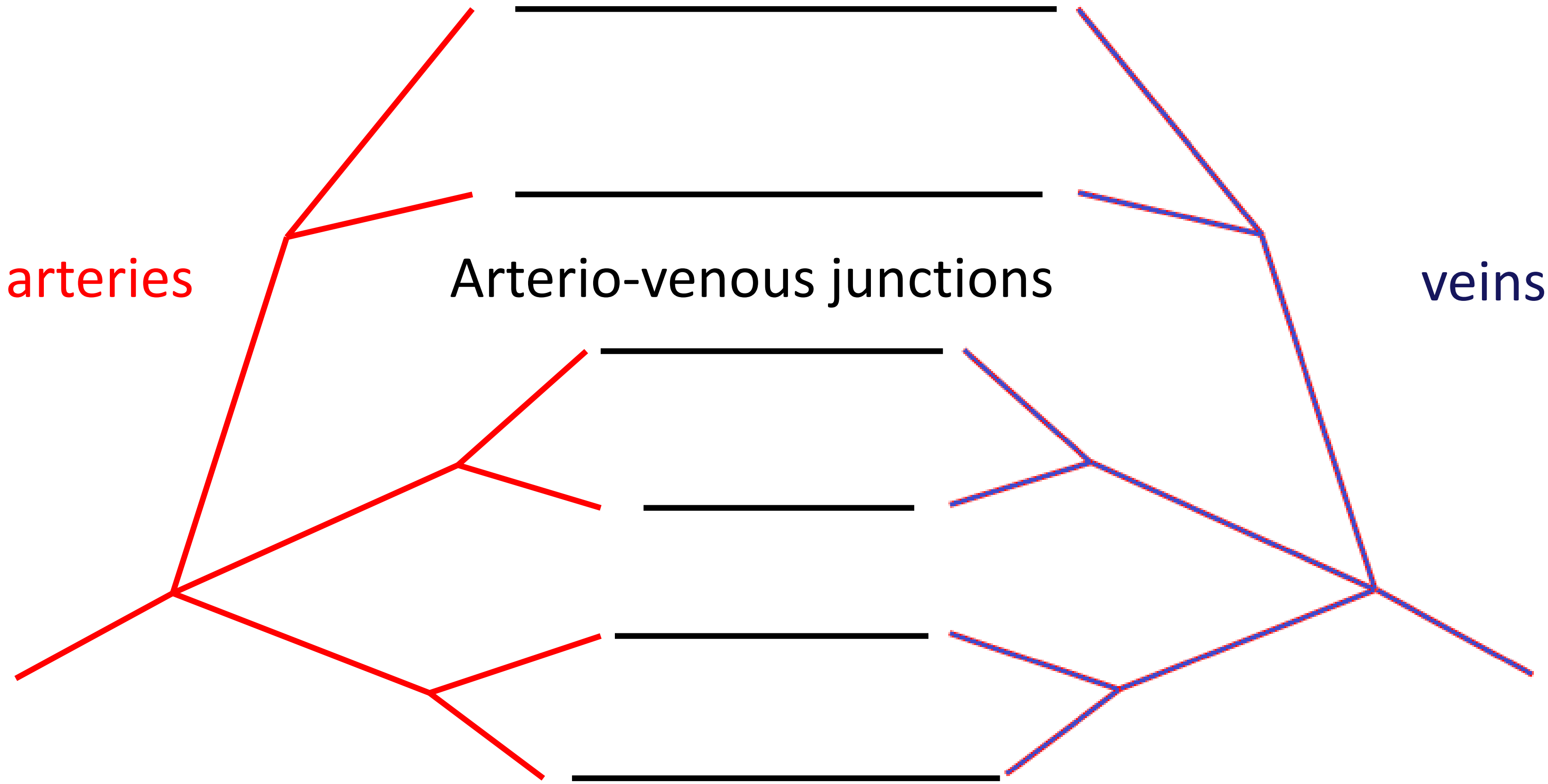
Clinical diagnostics:

- **Intravascular measurements**
- **Expensive transducer (single-use)**
- **Complicated analysis during multivessel coronary disease**
- **Complicated analysis during physical exercise**

Solution: Computational assessment of FFR on the basis of individual non-invasively collected data (MRI/CT, angiography, arterial pressure, heart rate, …)

FYu Kopylov, AA Bykova, YuV Vassilevski, SS Simakov, Role of measurement of fractional flow reserve in coronary artery atherosclerosis, Terapevticheskii Arkhiv, 87(9):106-113, 2015

Features of coronary flow

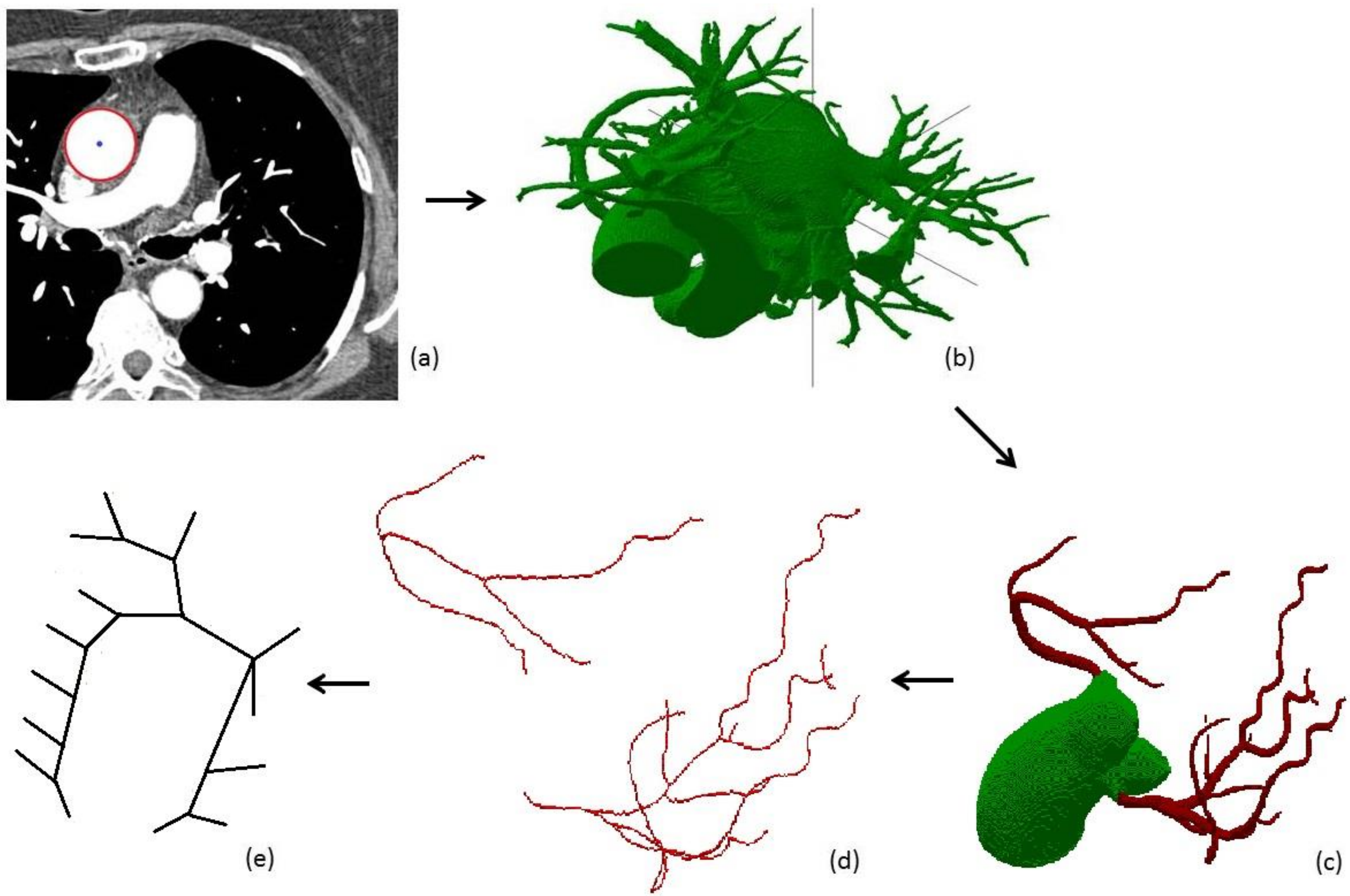


systole: 1) $P^{ext}(t,x)$ In the region of arterio-venous junctions (due to myocard contration)

2) Increased resistance of coronary arteries

Vis MA, Bovendeerd PH, Sipkema P, Westerhof N, Effect of ventricular contraction, pressure, and wall stretch on vessels at different locations in the wall. Am J Physiol Heart Circ Physiol 1997; 272: H2963–H2975.

Patient-specific identification of 1D structure of coronary network

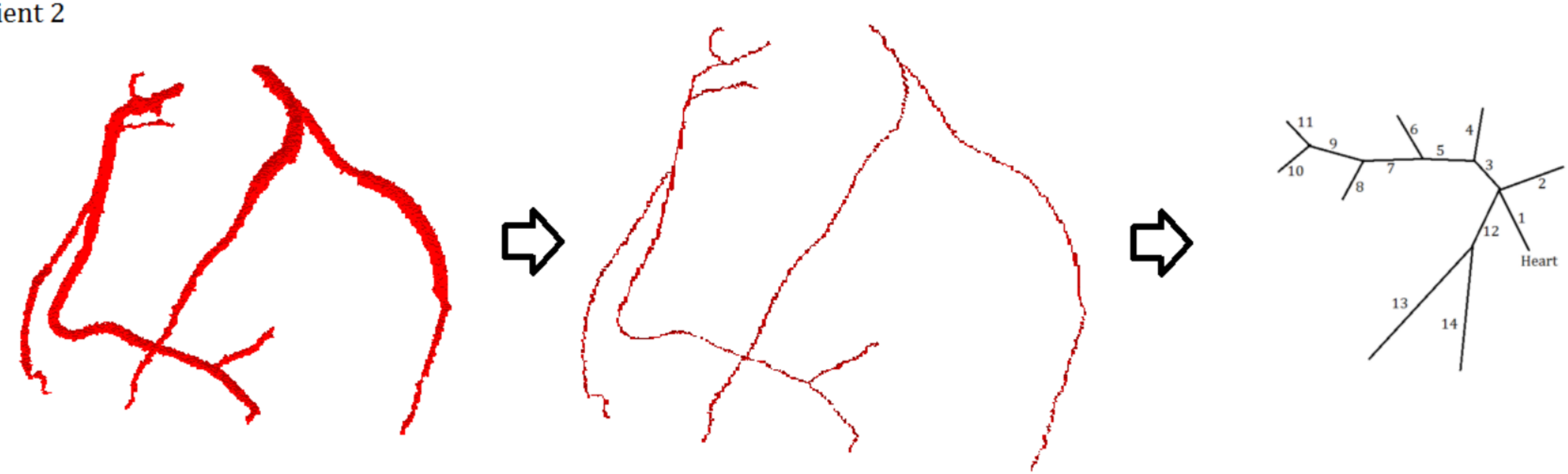


YuV Vassilevski, AA Danilov, TM Gamilov, YuA Ivanov, RA Pryamonosov, SS Simakov, Patient-specific anatomical models in human physiology, Russ. J. Num. Anal. Math. Mod., 2015

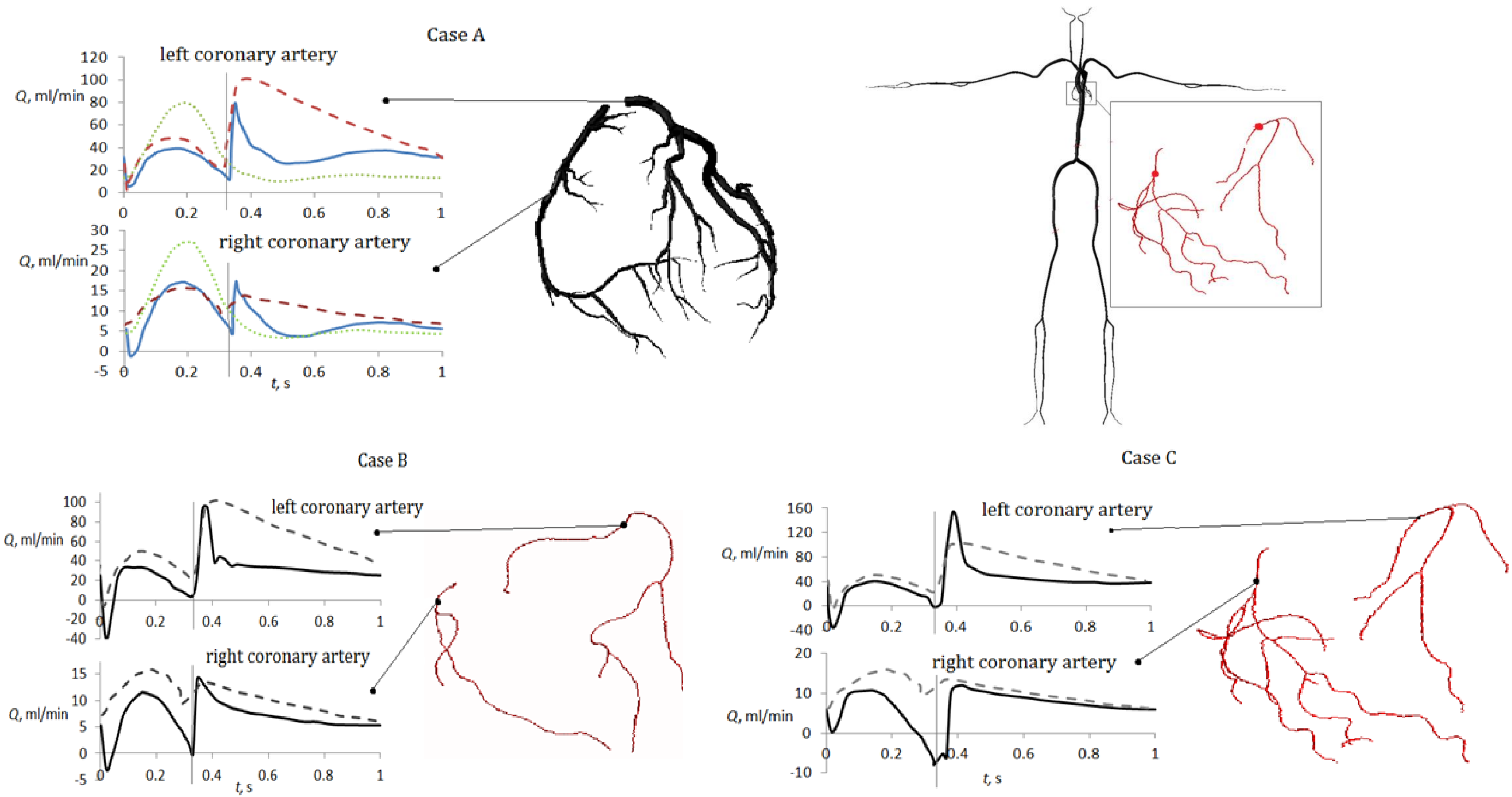
Fractional Flow Reserve
1D vascular domain reconstruction

Patient 1

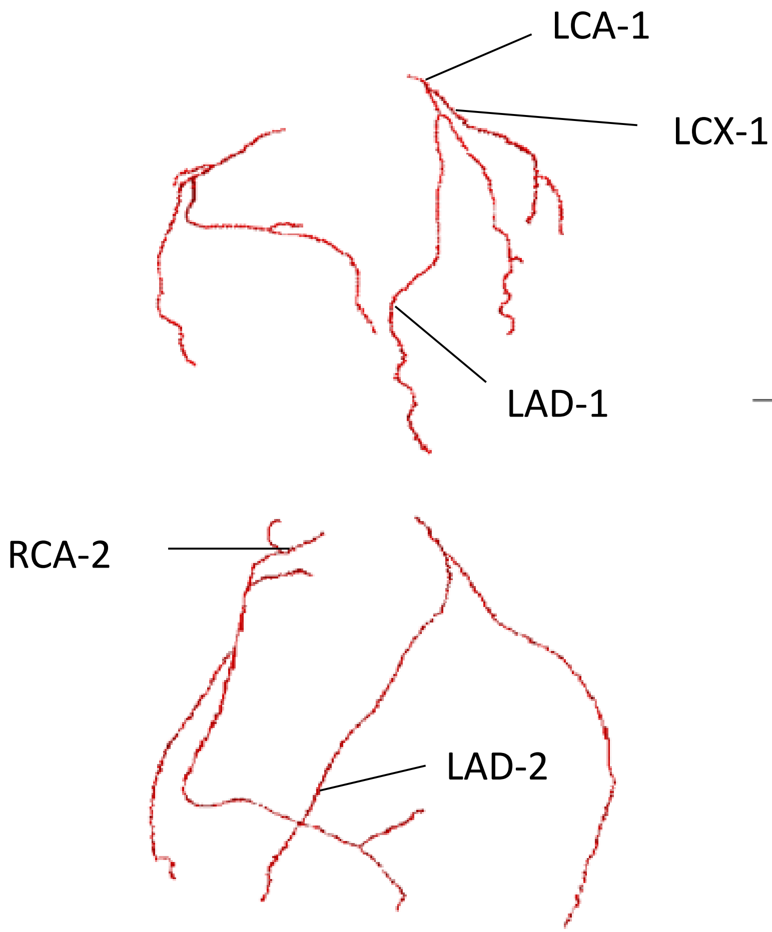
Patient 2



Simulation of coronary flow



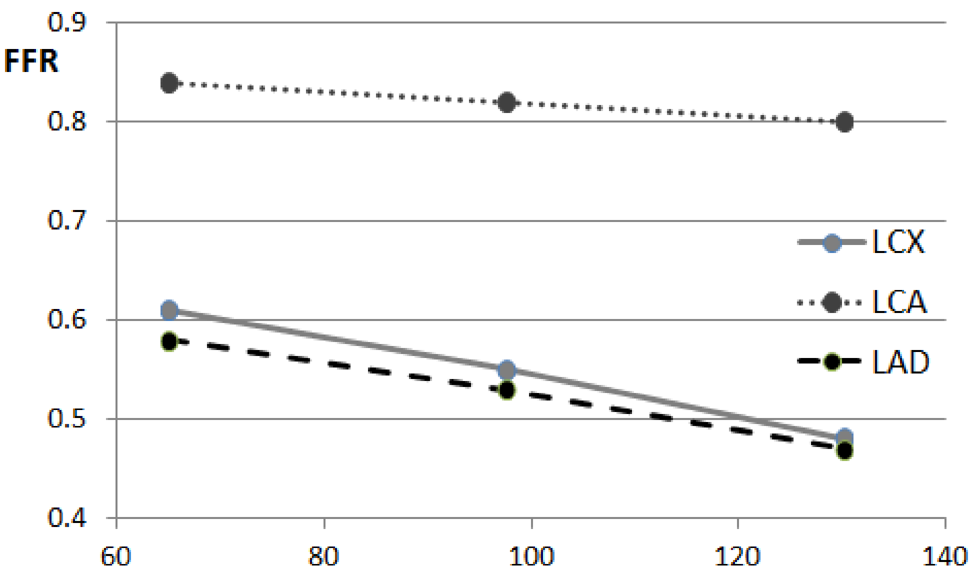
In Silico FFR simlation



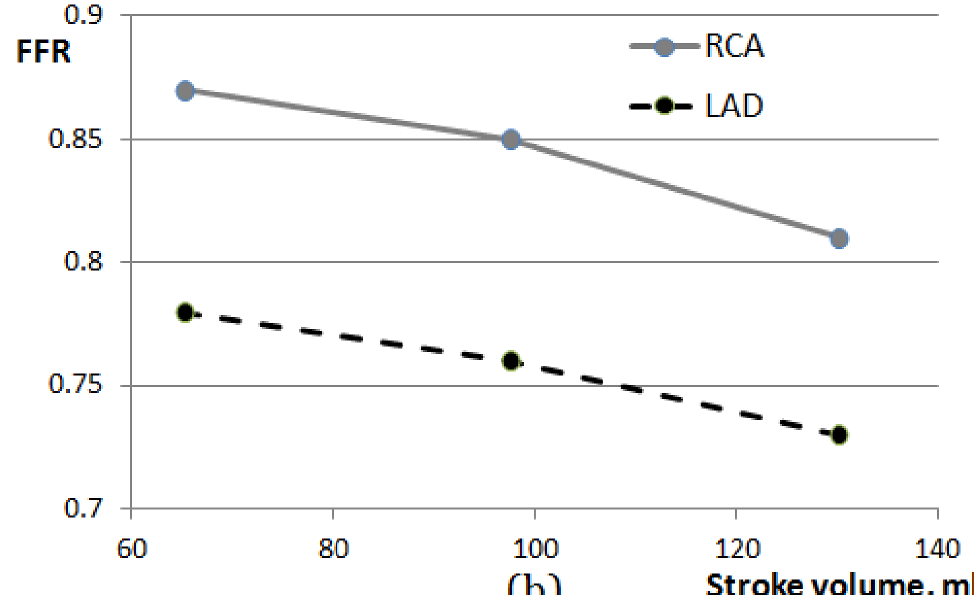
	Измеренный FFR	Рассчитанный FFR	Разница
LAD-1	0.51	0.58	+14%
LCA-1	0.72	0.84	+17%
LCX-1	0.59	0.61	+3%
LAD-2	0.74	0.78	+5%
RCA-2	0.93	0.87	-5%

T.Gamilov, Ph. Kopylov, R. Pryamonosov, S.Simakov, Virtual fractional flow reserve assessment in patient-specific coronary networks by 1D haemodynamic model, Russ. J. Num. Anal. Math. Mod., 2015

FFR during stroke volume increase



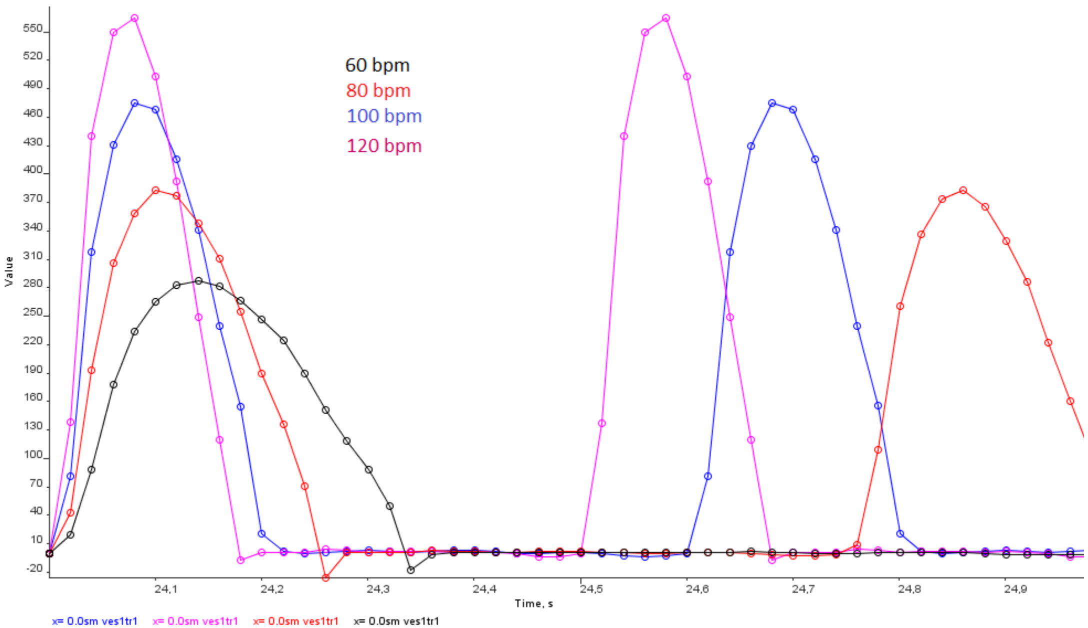
(a)

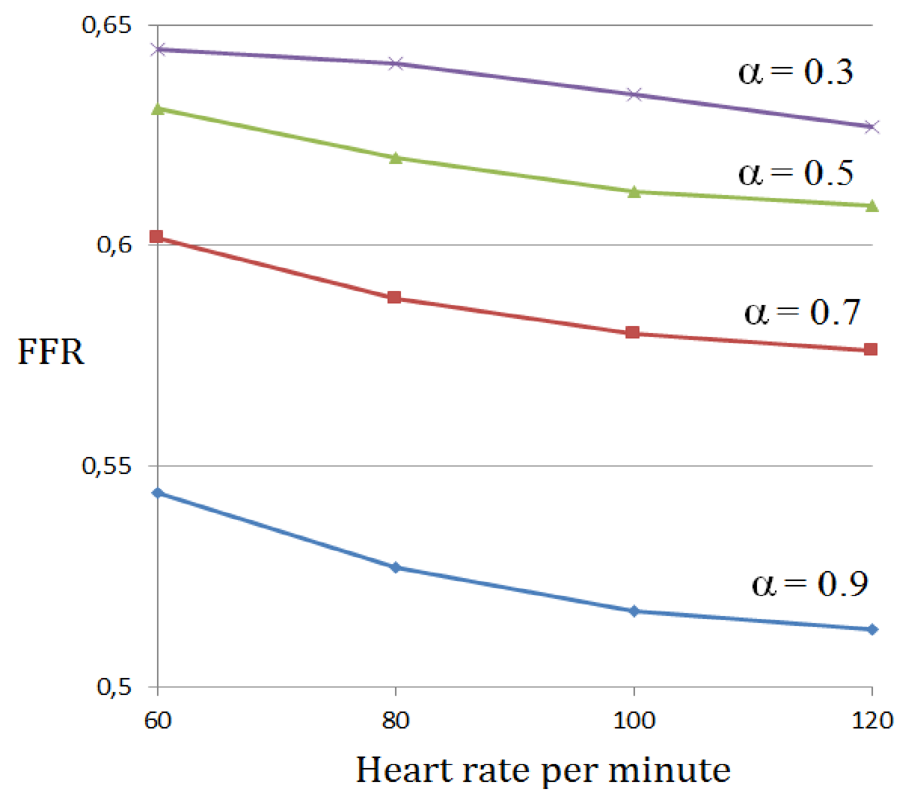


(b)

T.Gamilov, Ph. Kopylov, R. Pryamonosov, S.Simakov, Virtual fractional flow reserve assessment in patient-specific coronary networks by 1D haemodynamic model, Russ. J. Num. Anal. Math. Mod., 2015

FFR during stroke volume and heart rate increase





YuV Vassilevski, AA Danilov, TM Gamilov, YuA Ivanov, RA Pryamonosov, SS Simakov, Patient-specific anatomical models in human physiology, Russ. J. Num. Anal. Math. Mod., 2015

FFR: sensitivity analysis

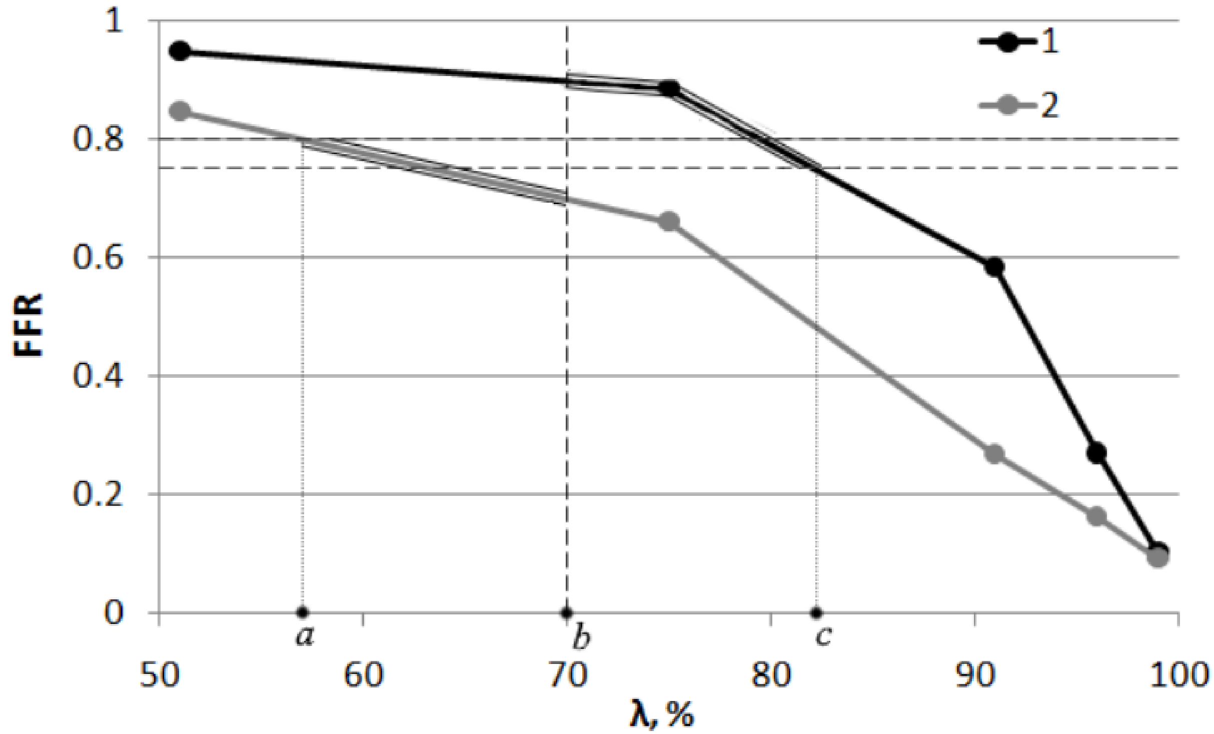


Figure 2. Comparison of FFR (7) for single stenosis of the same degree λ in LAD. Curve 1 corresponds to LAD with $d_{LAD} = 3mm$, curve 2 corresponds to LAD with $d_{LAD} = 2mm$.

S.Simakov, T.Gamilov, Ph. Kopylov, Yu. Vassilevski, Computational study of multivessel coronary disease: haemodynamic significance of stenoses in simulation, Bulletin of Experimental Biology and Medicine, 2016

FFR: sensitivity analysis

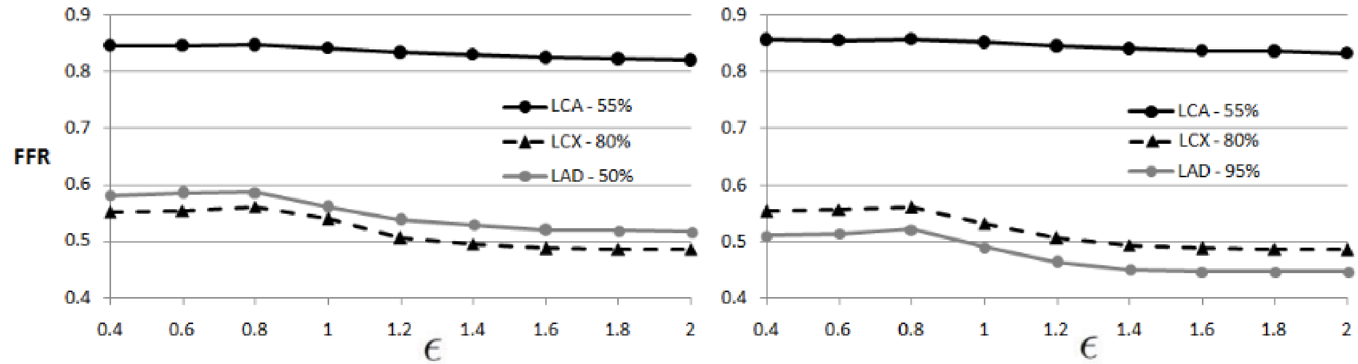


Fig. 2. Calculated FFR for different values of $c_k . c_k$ for all vessels were multiplied by ϵ. Left: patient-specific case (see Fig. 1); right: stenosis in LAD increased to 95%

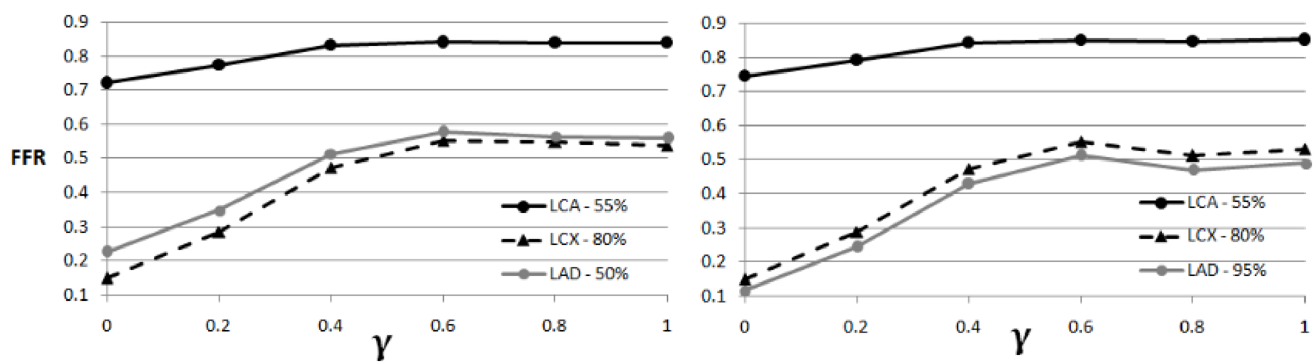
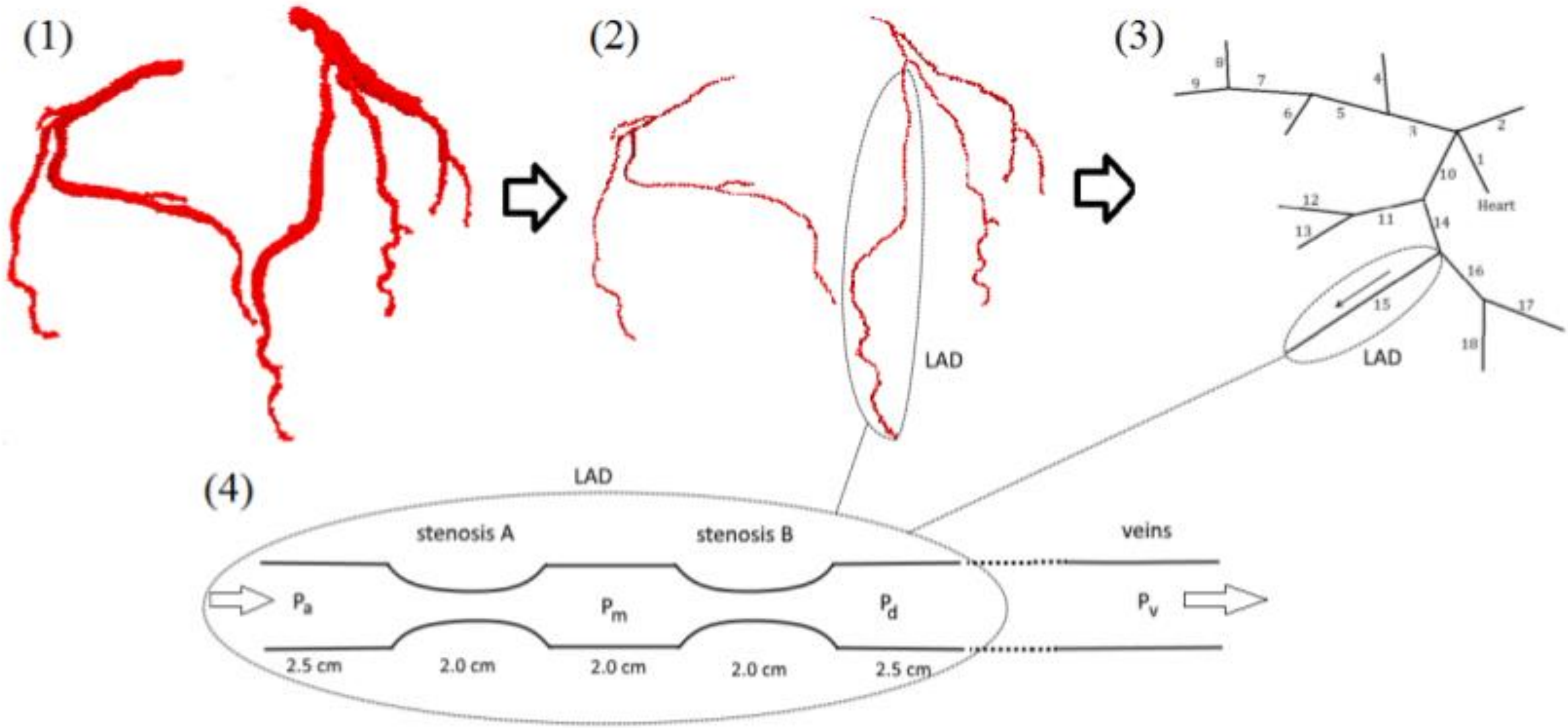


Fig. 3. Calculated FFR for different regimes of autoregulation (values of γ). $gamma = 1$ — normal autoregulation, $gamma = 0$ — absence of autoregulation. Left: patient-specific case (see Fig. 1); right: stenosis in LAD increased to 95%

T.Gamilov, Ph. Kopylov, S.Simakov, Computational Simulations of Fractional Flow Reserve Variability, Proceedings of ENUMATH 2015, 2016

FFR in multivessel coronary disease

$$FFR_A^{pred} = \frac{P_d - (P_m/P_a)P_v}{P_a - P_m + P_d - P_v}, \quad FFR_B^{pred} = 1 - \frac{(P_a - P_v)(P_m - P_d)}{P_a(P_m - P_v)}$$



S.Simakov, T.Gamilov, Ph. Kopylov, Yu. Vassilevski, Computational study of multivessel coronary disease: haemodynamic significance of stenoses in simulation, Bulletin of Experimental Biology and Medicine, 2016

FFR in multivessel coronary disease

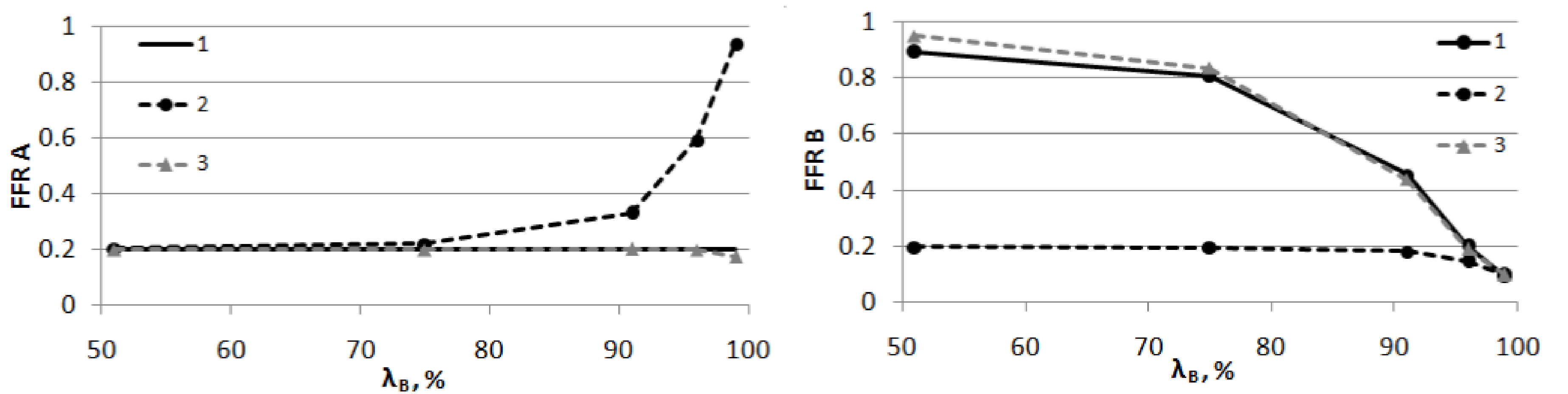
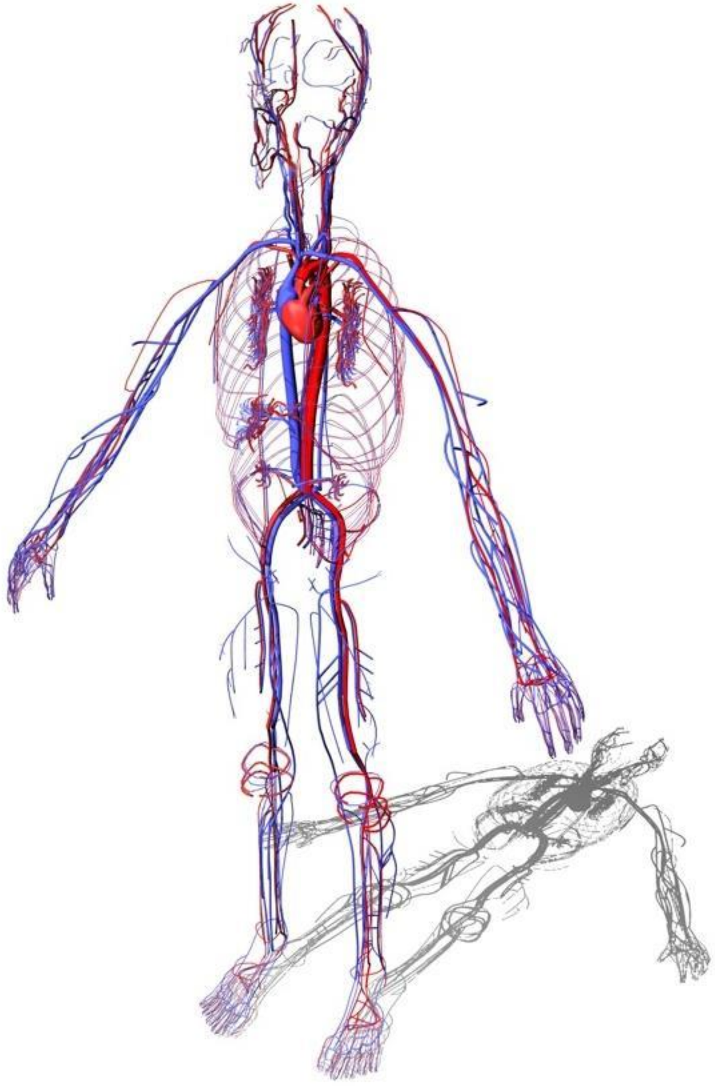


Figure 3. Comparison of FFR for two serial stenoses calculated by (7) and (8) during λ_B variations. Left: FFR at stenosis A during variation of λ_B, curve 1 shows FFR_A for $\lambda_B = 0\%$ (single stenosis A), curve 2 shows FFR_A (7), curve 3 shows FFR_A (8); Right: FFR at stenosis B during variation of λ_B; curve 1 shows FFR_B for $\lambda_A = 0\%$ (single stenosis B), curve 2 shows FFR_B (7), curve 3 shows FFR_B (8).

S.Simakov, T.Gamilov, Ph. Kopylov, Yu. Vassilevski, Computational study of multivessel coronary disease: haemodynamic significance of stenoses in simulation, Bulletin of Experimental Biology and Medicine, 2016

Cerebral Flow: Carotid Stenosis Treatment

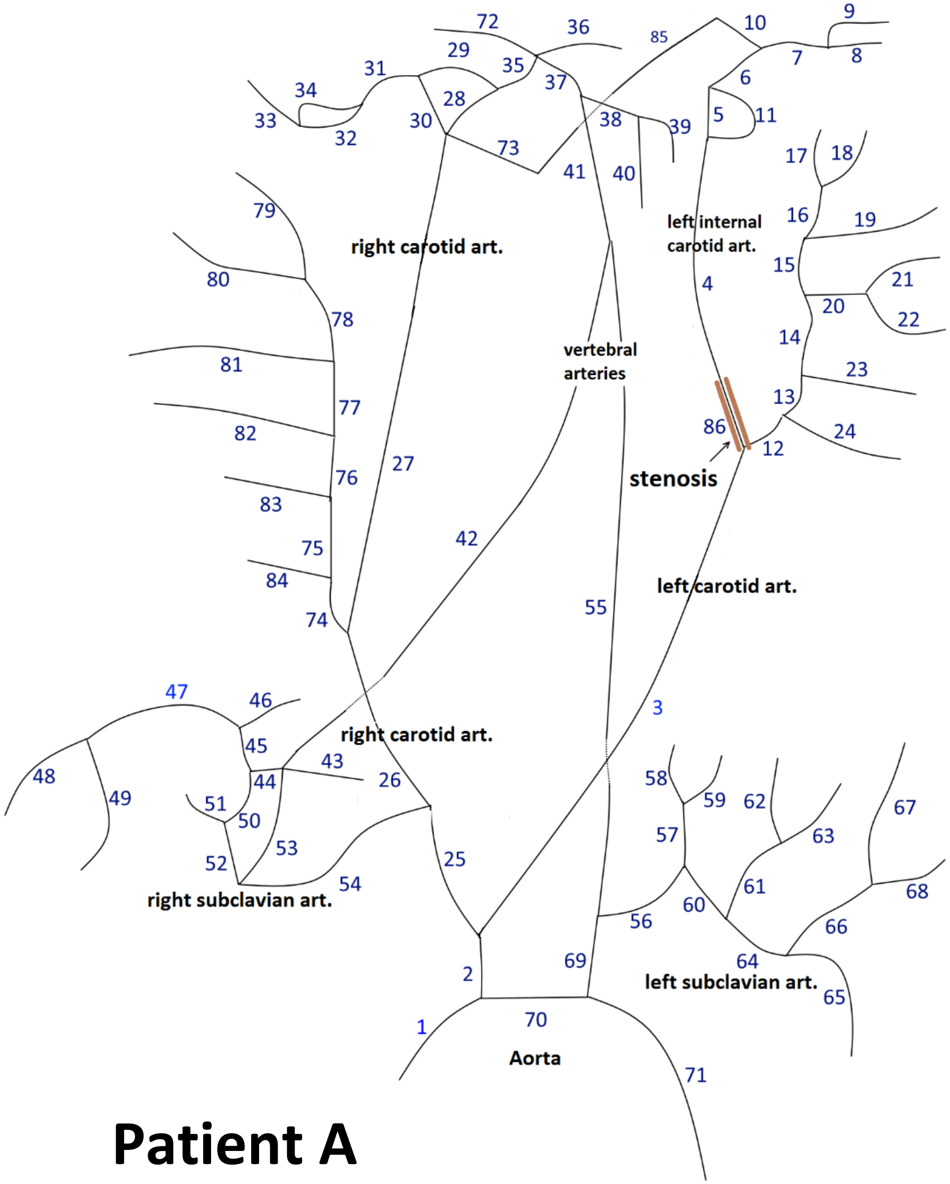


Reconstruction

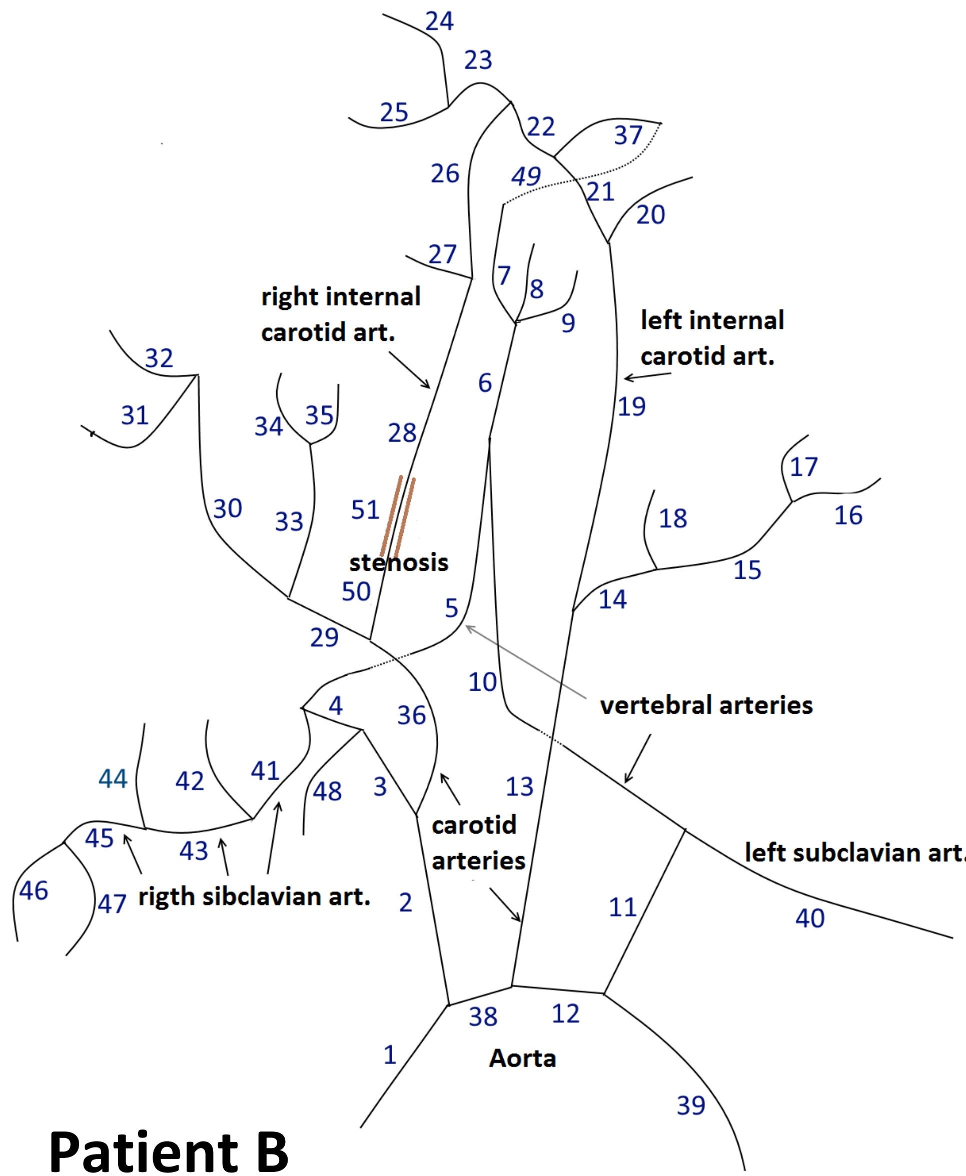
Franghi vesselnes filter

Thanks to Roman Pryamonosov, INM RAS

Cerebral Flow
1D vascular domain reconstruction



Patient A



Patient B

Cerebral Flow

Before treatment (with stenosis)

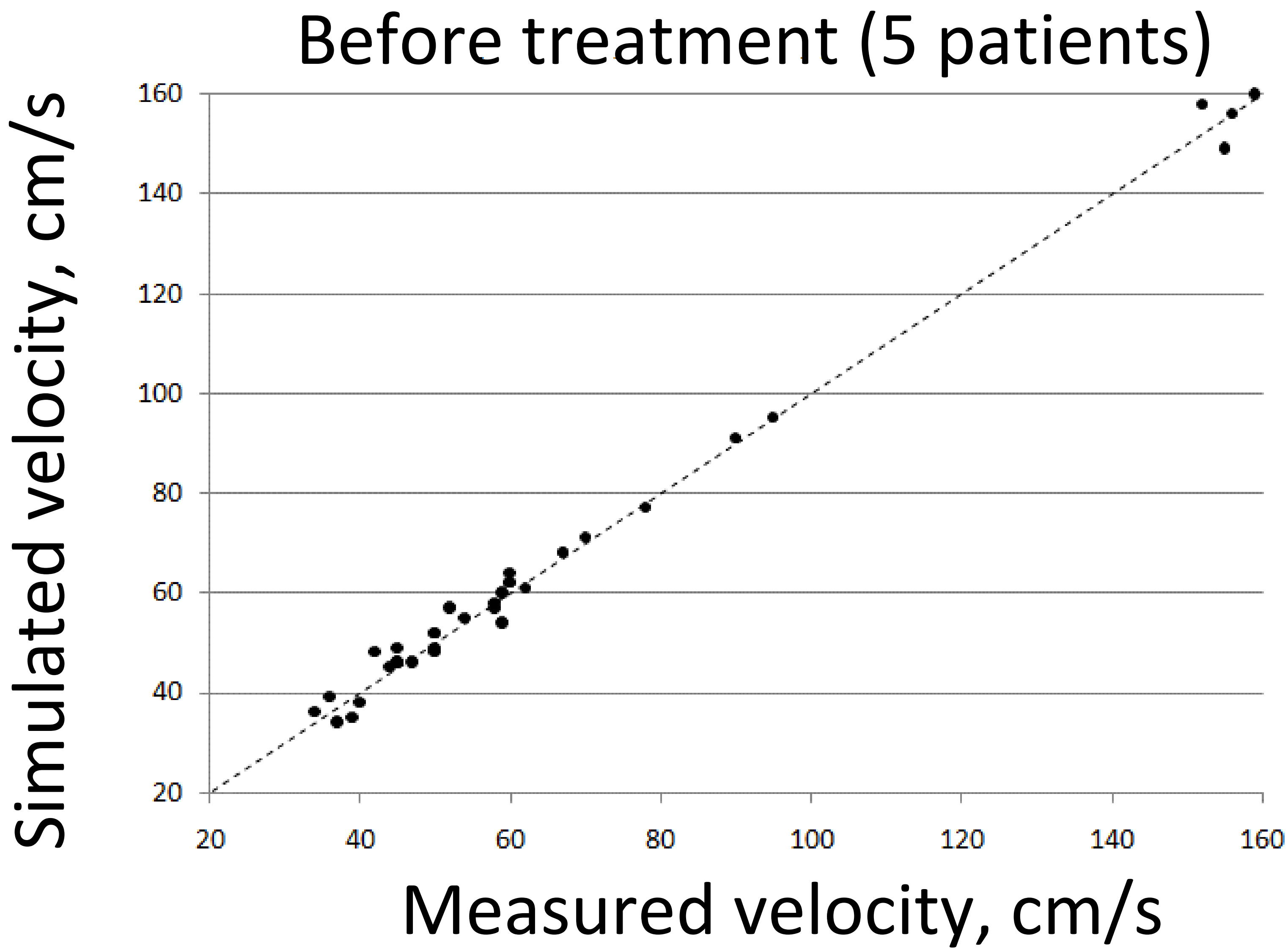
		Left			Right		
		model (cm/s)	measured (cm/s)	error (%)	model (cm/s)	measured (cm/s)	error (%)
Patient A	Common Carotid Art. (No 26, 3)	50	55	*9*	51	54	*5,5*
	Internal Carotid Art. (No 27, 86)	72	67	*7*	240	220	*10*
Patient B	Common Carotid Art. (No 13, 36)	51	58	*12*	60	56	*7*
	Internal Carotid Art. (No 19, 28)	130	96	*35*	58	55	*5*

Cerebral Flow

After treatment (stenting)

	Vessel's index		Velocity, cm/s		
	Patient A	Patient B	Patient A	Patient B	Norm
Common Carotid Art.	3, 26	2, 13	60	59	50-104
Internal Carotid Art.	27, 86	19, 28	48	60	32-100
External Carotid Art.	74-75, 12-13	29-31, 14-16	60	90	37-105
Vertebral Art.	42, 55	5, 10	50	35	20-61
Subcluvian Art.	54-52-50, 56-60-64	40, 3-4, 41-43-46	98	95	60-150

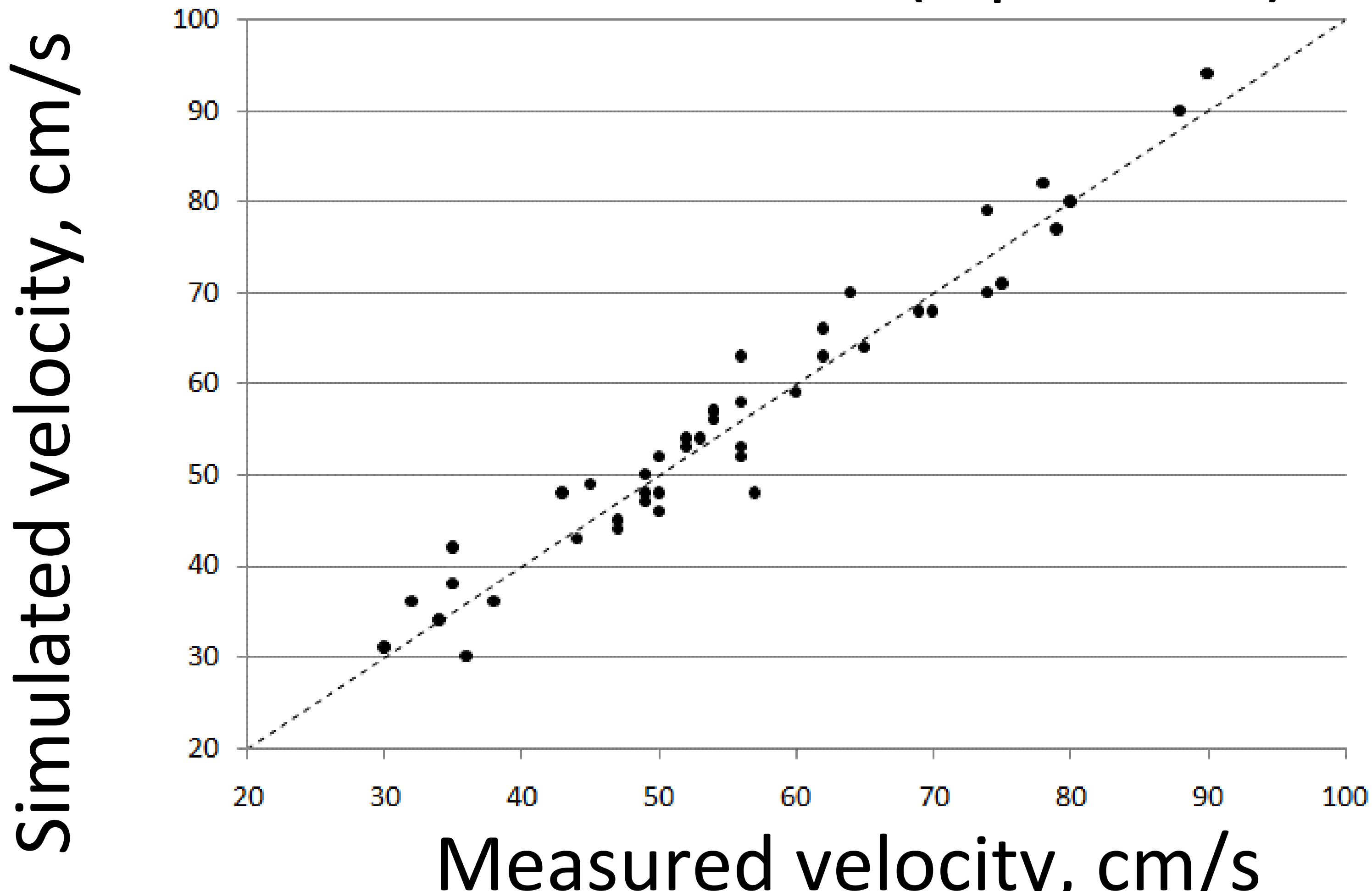
Cerebral Flow



Relative error: average – 4%; maximum – 16%

Cerebral Flow

After treatment (5 patients)



More details will be given by Timur Gamilov (next talk)

Relative error: average – 6%; maximum – 20%

Conclusions

- Adequate tool for predictive assessment of post surgical blood flow after stenting was developed
- Successful patient-specific simulations cover
  - ✓ Femoral artery stenting
  - ✓ Virtual FFR assessment
  - ✓ Carotid artery stenting
- Automatization of the presented method and validation with more clinical cases are required to translate the results to the bedside

Thank You!

<u>Special thanks</u>

Timur Gamilov

Roman Pryamonosov

Dmitry Burenchev

Philippe Kopylov