A technology non-invasive assessment of the fractional flow reserve

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The Week of Applied Mathematics and Mathematical Modelling

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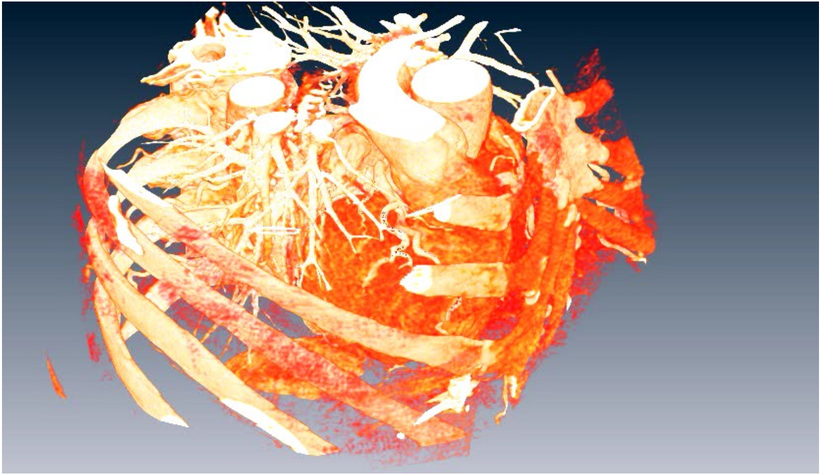
Joint work with colleagues from Sechenov University:

- Timur Gamilov,
- Sergey Simakov,
- Roman Pryamonosov,
- Alexander Danilov,
- Darya Gognieva,
- Philipp Kopylov

Coronary arteries



Motivation

Ischemic heart disease is caused by

- pathology of microvasculature (therapy)
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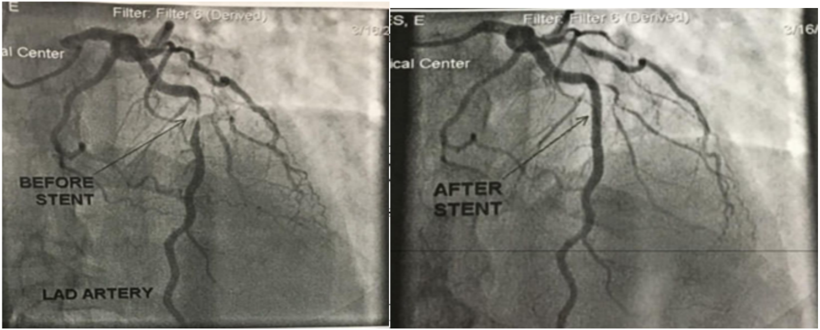

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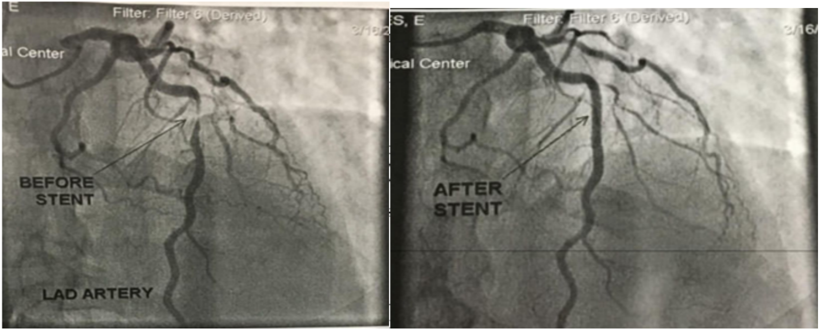
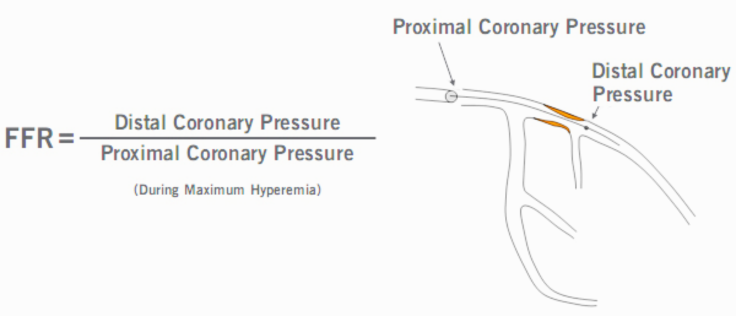


Indication for revascularization

- before 2014: Vascular occlusion factor (relative lesion cross-sectional area) $VOF > 0.7$
- after 2014: Fractional flow reserve $FFR < 0.75$

2014 ESC/EACTS Guidelines on myocardial revascularization. *Eur.Heart J*, 2014 **35** (37)

Fractional flow reserve (FFR)



Clinical practice: endovascular intervention, expensive transducer

Pijls NH, Sels JW., Functional measurement of coronary stenosis. *J.Am. Coll. Cardiol.*, 2012 **59** (12)
Kopylov Ph., Bykova A., Vassilevski Yu., Simakov S. Role of measurement of fractional flow reserve (FFR) in coronary artery atherosclerosis. *Therapeutic archive*, 2015 **87** (9)

Virtual fractional flow reserve FFR_{CT}

- Hemodynamic simulation based on personalized data:
  - Computed Tomographic Coronary Angiography (DICOM)
- $FFR_{CT} = \frac{\overline{P}_{dist}}{\overline{P}_{aortic}}$

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- $FFR_{CT} = \frac{\overline{P}_{dist}}{\overline{P}_{aortic}}$
- Advantages of FFR_{CT}
  - non-invasivity
  - physiological significance of each of multiple lesions
  - virtual stenting
  - applicability to any segment of the coronary tree

Virtual fractional flow reserve from 3D simulations

3D Navier-Stokes equations

HeartFlow has gained U.S. Food and Drug Administration (FDA) approval for the use of FFR_{CT} as a class II Coronary Physiologic Simulation Software Device

Morris P. et al. “Virtual” (Computed) Fractional Flow Reserve: Current Challenges and Limitations. *J Am Coll Cardiol Intv.* 2015, **8** (8)

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Difficulties of FFR_{CT} evaluation by 3D simulations:

- boundary conditions for 3D problem
- simulation time
- frozen vascular walls (physics?) or FSI (expensive,coefficients?)

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Alternative approach: 1D hemodynamics (1D flows in elastic tubes)

Hemodynamic equations

Mass and momentum balance

$$\begin{aligned} \partial S_k/\partial t + \partial(S_k u_k)/\partial x &= 0, \\ \partial u_k/\partial t + \partial\left(u_k^2/2 + p_k/\rho\right)/\partial x &= -\frac{8\pi\mu u_k}{S_k}, \end{aligned}$$

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

S.S.Simakov, A.S.Kholodov. Computational study of oxygen concentration in human blood under low frequency disturbances. *Mathematical Models and Computer Simulations*, 2009 **1** (2)

Hemodynamic equations

At the vessels junctions continuity of the total pressure and mass conservation

$$p_i\left(S_i\left(t,\tilde{x}_i\right)\right)+\frac{\rho u_i^2\left(t,\tilde{x}_i\right)}{2}=p_j\left(S_j\left(t,\tilde{x}_j\right)\right)+\frac{\rho u_j^2\left(t,\tilde{x}_j\right)}{2},$$

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

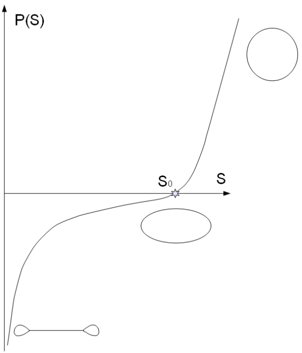
$\varepsilon=1, \tilde{x}_k=L_k$ for incoming tubes, $\varepsilon=-1$, and $\tilde{x}_k=0$ for outgoing tubes

S.S.Simakov, A.S.Kholodov. Computational study of oxygen concentration in human blood under low frequency disturbances. *Mathematical Models and Computer Simulations*, 2009 **1** (2)

Hemodynamic equations

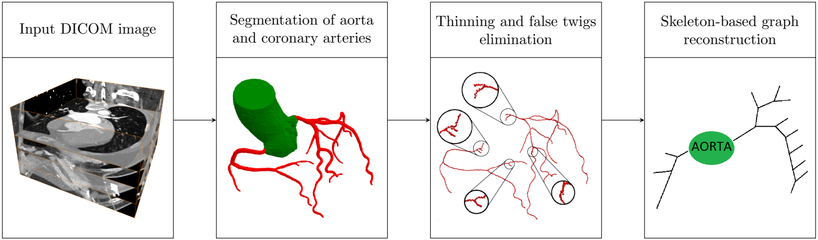
Elasticity of the tube wall:

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



Vassilevski Yu., Salamatova V., Simakov S. On the elastisity of blood vessels in one-dimensional problems of hemodynamics. J. Computational Mathematics and Mathematical Physics, V.55, No.9, p.1567-1578, 2015.

Automatic segmentation and skeletonization



Overview of pipeline for automatic network reconstruction

A. Danilov, et al. Methods of graph network reconstruction in personalized medicine. IJNMBE, 2016

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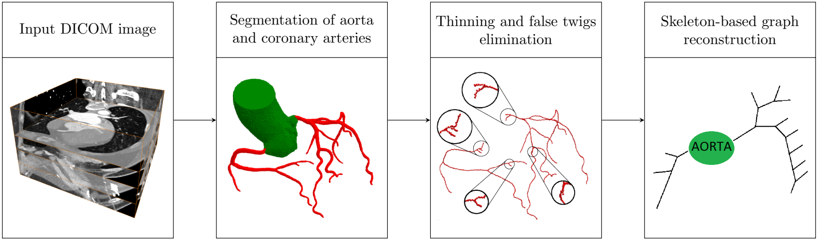

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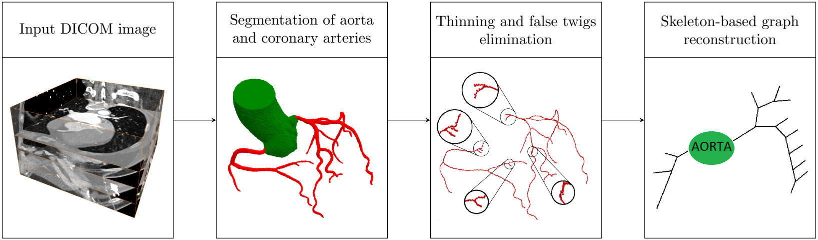
Aorta segmentation by isoperimetric distance trees

L. Grady. Fast, quality, segmentation of large volumes – Isoperimetric distance trees. ECCV, 2006.

Automatic segmentation and skeletonization



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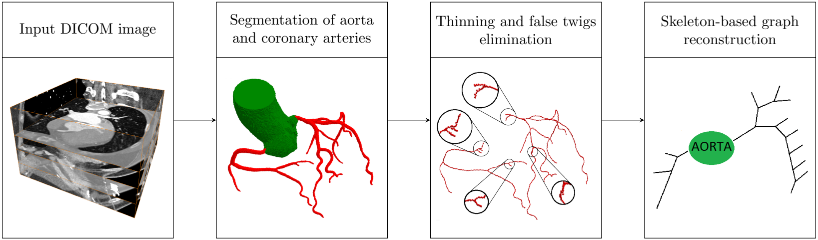
Frangi vesselness filter generates bigger values inside bright tubular structures

A. Frangi, W. Niessen, K. Vincken, and M. Viergever. Multiscale vessel enhancement filtering. MICCAI, 1998.

Automatic segmentation and skeletonization



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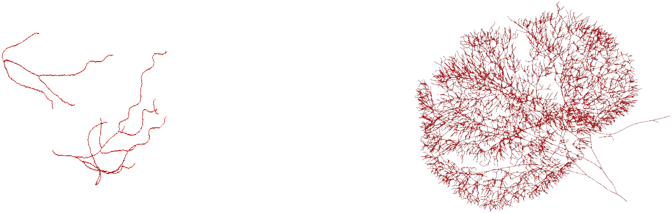
Skeletonization produces vascular 1D computational network

C. Pudney. Distance-ordered homotopic thinning: A skeletonization algorithm for 3D digital images.CVIU, 1998.

Skeletonization efficiency



Skeletons of a coronary tree and of a micro-CT of vascular corrosion cast of rabbit kidney provided by J. Alastruey,

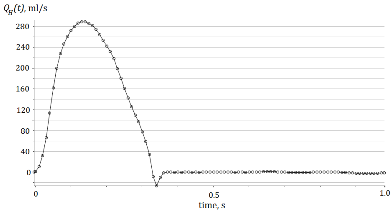
Department of Bioengineering, King's College London, UK

	Case 1	Rabbit kidney
Resolution	$512 \times 512 \times 248$	$2000 \times 1989 \times 910$
Distance map	0.20 sec	58.12 sec
Thinning	0.79 sec	526.98 sec
False twigs cleaning	0.15 sec	16.61 sec
Graph construction	0.13 sec	12.27 sec
Skeleton segments	22	4302

Coronary hemodynamics in silico

T.Gamilov, Ph.Kopylov, R.Pryamonosov, S.Simakov. Virtual Fractional Flow Reserve Assesment in Patient-Specific Coronary Networks by 1D Hemodynamic Model. *Russ. J. Numer. Anal. Math. Modelling*, 2015 **30** (5)

- On arterial entry unsteady flux (1Hz, 65ml) is scaled to HR and systolic/diastolic pressures, venous pressure (12 mmHg) is given



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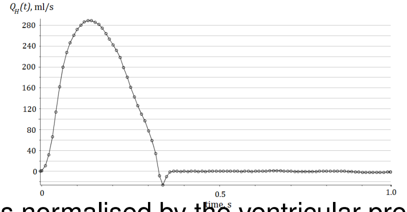
- On arterial entry unsteady flux (1Hz, 65ml) is scaled to HR and systolic/diastolic pressures, venous pressure (12 mmHg) is given
- Compression of arteries during systola by myocard: $p_{*k} = P^{cor}_{ext}(t)$, $R^{syst}_k = 3R^{diast}_k$



P^{cor}_{ext} is normalised by the ventricular pressure

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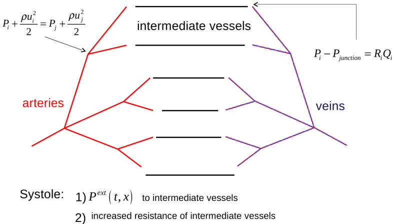
- Resistance of microcirculation
  $p_k\left(S_k\left(t, \tilde{x}_k\right)\right) - p_{veins} = R_k S_k\left(t, \tilde{x}_k\right) u_k\left(t, \tilde{x}_k\right)$



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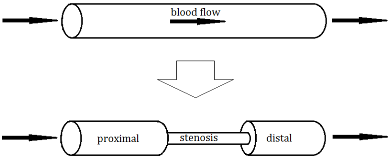
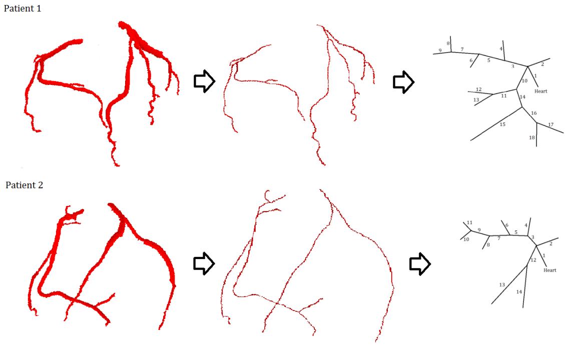
- Stenosis with fraction α: $S_0^{st} = (1-\alpha)S_0$



Computation of virtual fractional flow reserve



reconstructed arterial part based on two anonymous patient-specific data sets

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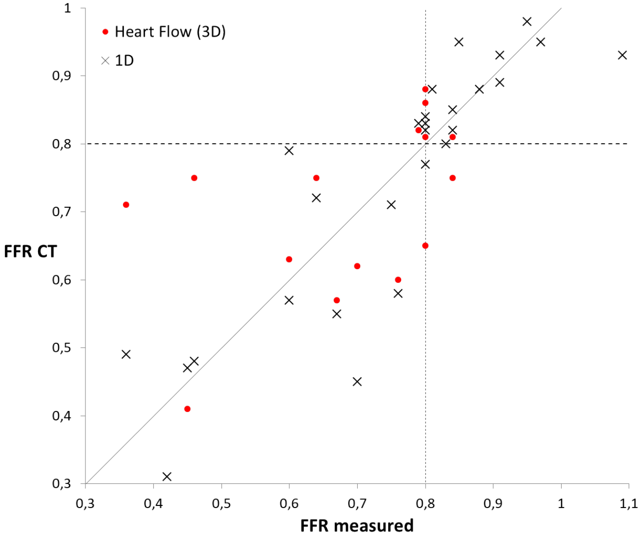

Non-invasive coronary CT angiography-derived fractional flow reserve (FFR): A benchmark study comparing the diagnostic performance of four different computational methodologies. *Int.J.Num.Meth.Biomed.Engng.*2019;e3235.

Open issues

- Intensive validation for
  1D $FFR_{CT} \leftrightarrow$ FFR

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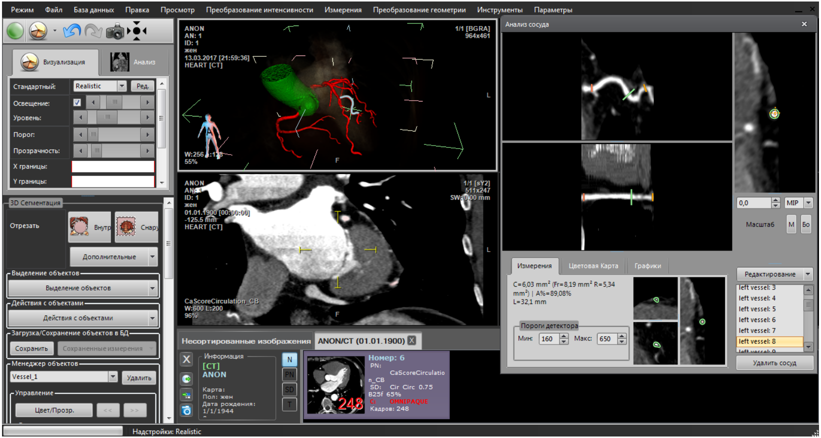
- Concept of FFR for multiple stenoses

FFR$_{CT}$ within Multivox toolbox

Medical computer systems, Lomonosov Moscow State Univ.



Conclusion

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Thank you for your attention!